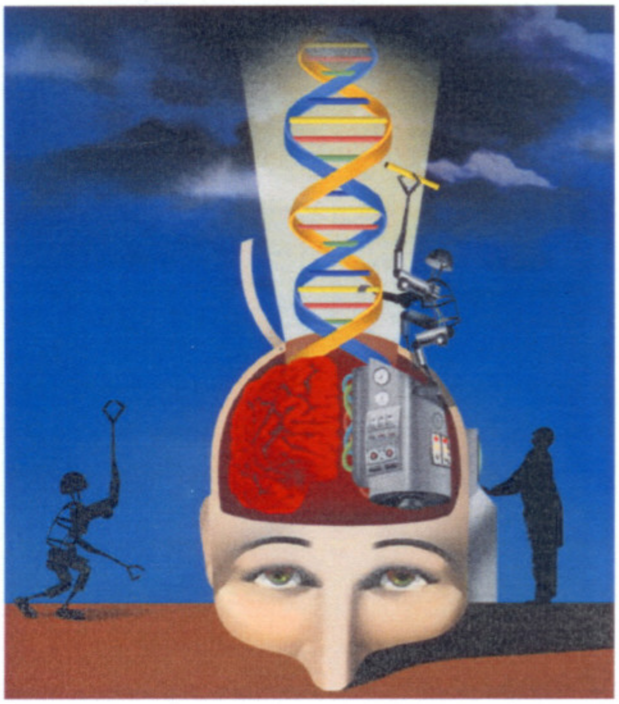
theguardian

Body of research

We may soon be able to control mechanical limbs just by using our brains, grow a new heart after a heart attack or replace faulty genes. Ian Sample takes a look at the future of our species

Ian Sample
guardian.co.uk, Sunday 20 November 2011



With the use of brain-machine-brain implants, it is plausible to go beyond what we define as human. Illustration: Brett Ryder

Miguel Nicolelis, a neuroengineer at Duke University Medical Center in Durham, North Carolina, will be watching the opening ceremony of the Brazilian World Cup in 2014 more closely than anyone. Amid the spectacle of the event that will draw millions of viewers around the world will be a very public unveiling of his greatest work.

One of the highlights of the ceremony will see the Brazilian team walk on to the pitch for the first time in the tournament, striding out behind two quadriplegic teenagers. Nicolelis then wants the teenagers, wearing exoskeletons controlled by his technology, to approach and kick the ball.

At the heart of Nicolelis's work is a device called a brain-machine-brain interface (BMBI). These can replace the damaged spinal nerves that leave people paralysed by sending information back and forth between their brains and robotic machinery. In this case, the wearers will control their exoskeletons with their minds alone.

The idea may sound ambitious, but Nicolelis has support from the Brazilian government and has teamed up with researchers at the Technical University in Munich to build a prototype exoskeleton, a mechanical framework that surrounds and moves the body using motors.

Endowing the exoskeleton with sensory feedback should make the system easier to control, because the wearer will be able to actually feel the ground beneath their feet.

"The patient will be able to use their brain to control their movement, but they could also get sensations back from their legs, arms and hands," said Dr Nicolelis.

"The idea is to have the first demonstration at the World Cup and then, a few years later, we hope to be able to unveil a more advanced exoskeleton," says Nicolelis, who hails from São Paulo, the country's largest city. "It's like the Brazilian moonshot."

"One exoskeleton will be for the waist down, the other will be a whole-body system. At the moment it is more conspicuous than we would want, but even the first generation is not going to be like Robocop. In the future, we want something more like a vest, and the technology is going to get there, no doubt about it," he says.


The exoskeleton provides hope for people paralysed by spinal injury. Photograph: Getty

The road to a fully functioning, mind-controlled exoskeleton that can bring movement back to the paralysed will be hard, but recent experiments at Nicolelis's lab point to ways that the technology might transform the body even further. With the use of brain-machine-brain implants, it is plausible to go beyond what we define as human.

Preliminary work by Nicolelis suggests that it might be possible to equip animals, and perhaps ultimately humans, with additional senses.

For example, an infrared sensor could be worn that senses heat in the environment and relays this information directly into the brain.

Encoded in a meaningful way our brains might well make sense of the information and use it like any other sense.

The prospect of seeing the world in infra-red might not appeal to many people, and it is hard to see much call for brain implants that pick up other information that passes us by all the time, such as that carried by ultrasonic or subsonic sound waves. But this is taking a very limited view of the possibilities. Sensors on our heads or bodies, or even at remote sites, might be designed to pick up and combine all manner of information in the world around us, which could be fed wirelessly into our brains as entirely new sensations.

Nicolelis's work hints at even more extraordinary possibilities. He says the implants can "effectively liberate the brain from the physical constraints of the body". There's no reason why, for example, an exoskeleton might control only the usual number of human limbs. "We could have four legs or four arms on an exoskeleton and we would make the brain assume that is the natural body configuration," he says. "That is how far you can go."

With the use of BMBIs, it may even be possible to overcome some of the damage inflicted by brain injuries and neurodegenerative diseases. If the brain is as flexible as Nicolelis believes, BMBIs might connect healthy, functioning parts of the brain, and help them work around those regions of our grey matter that are destroyed or failing.

The art of hooking up brains to machines and machines to brains is moving forwards at an impressive pace, but other areas of medical research seem poised to make their own dramatic impacts on what it means to be human. Swift advances in genetics and cell biology have made plausible the genetic modification of our hearts and minds, and paved the way for genetics to enhance our natural selves.

One reason that heart and brain diseases take such a toll on public health is that cells in those organs barely regenerate in adult humans. What ability there is for heart muscle cells to replicate and so repair, for example, is paltry compared to the damage done by a heart attack, which can destroy a billion cells in one destructive blow. While more people survive heart attacks than ever before, the damage they are left with never heals.

Our hearts weren't always so inflexible. In the womb, heart muscle cells called cardiomyocytes divide and multiply quite happily, to make the chambers, valves and blood vessels a healthy person requires. But the cells lose this capability soon after birth, and from that moment on, any injury to the heart is beyond the body's natural healing mechanisms.

At Mount Sinai School of Medicine in New York, Hina Chaudhry, director of cardiovascular regenerative medicine, has found what might be a way around the problem. She works on a gene called cyclin A2, which acts as the master regulator of heart cell division. When cyclin A2 falls silent in heart cells shortly after birth, they abruptly lose their ability to divide.

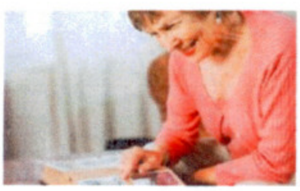
Chaudhry's team wondered what might happen if they genetically modified the heart, temporarily switching cyclin A2 back on in heart cells. To find out, they invented a gene therapy that carries cyclin A2 directly to the organ. The hope was that it might help repair some of the damage caused by a heart attack. In a recent trial in pigs the therapy looked promising, boosting the amount of blood the animals could pump after having a heart attack. Close inspection of animals' hearts revealed signs that heart cells had grown back to repair the organ.

Chaudhry's team is now testing a version of the gene therapy that will be suitable for humans, ahead of applying for permission to launch the first clinical trial. "The exciting thing about this is that if it works in the pig heart, it will work in the human heart. On a physiological and structural level the pig heart is almost identical to the human heart," she says.

Protection for brains

Similar thinking has prompted scientists to wonder whether genetically modifying our brains might protect them against neurodegenerative diseases, which, as the population rises, are becoming an ever greater burden on society. Given the complexity of the brain and our ignorance of its workings, hopes of a cure are exceptionally slim, but there are hints that it may be possible to slow the steady wasting away of brain cells that defines some dementia.

In a trial launched last year by Mark Tuszynski, director of the Centre for Neural Repair at the University of California in San Diego, patients with Alzheimer's disease received injections directly into their brains of a gene called NGF, or nerve growth factor. In a previous small-scale trial, the gene appeared to boost the connections between neighbouring brain cells and slow patients' cognitive decline.


Some scientists believe genetically modifying our brains might protect against neurodegenerative diseases. Photograph: Image Source/Getty Images/Image Source

The difficulty in treating Alzheimer's is that it destroys cells all over the brain. Tuszynski's approach targets a small group of brain cells called cholinergic neurons that extend their long, thin axons throughout the cortex. "These cells influence the activity of neural networks throughout the cortex and their early degeneration in Alzheimer's disease is thought to contribute considerably to cognitive decline," Tuszynski says. "We recognise we won't cure the disease, but if we can improve the functional state of these cells, that could have an important clinical benefit for patients' quality of life." The trial is due to end in 2014.

While traditional gene therapies add extra genes to cells, a more recent technique called genome editing allows doctors to remove faulty genes and replace them with healthy copies. The technology, which uses specially designed enzymes called zinc finger nucleases to cut strands of DNA, is so precise it can be used to correct even single letter misspellings in an organism's genetic code.

If recent studies are any guide, genome editing could become an important tool for rewriting human genomes in the future, with all the possibilities that brings. In June, Katherine High at the children's hospital of Philadelphia used the technique to treat mice with the blood disorder haemophilia by rewriting the genetic code of liver cells in the animals soon after birth. The study was the first to demonstrate that a live animal could be treated for an illness by editing its genome.

Months later, researchers at the Sanger Institute in Cambridge applied genome editing to a human illness. In a biological tour de force, they took skin cells from a patient with liver disease, converted them into a stem cell-like state, corrected the genetic flaws in these cells that caused the disease, and transformed the cells back into liver tissue. Doctors did not implant the cells back into the patient because safety trials have not been done, but when injected into mice, the cells collected in the liver and worked just like healthy liver cells. The study points to a radical new way of healing our bodies.

"In five to 10 years we may be able to make tissues that can go back into the body," says David Lomas, a respiratory physician and deputy director of the Cambridge Institute for Medical Research, who took part in the Sanger Institute study. Rather than simply injecting these cells into the body, they might sit alongside organs, in porous bags that prevent them from going astray.

"In an ideal world you would take skin cells, reprogramme them, then grow them into different cell types and have them populate a scaffold to make an organ," Lomas says. "But right now that is the stuff of Star Trek."

The advantage of genome editing over other forms of gene therapy is that the faulty gene is corrected in its normal position, so all the biological machinery needed to switch on and regulate the gene is already in place. One issue that isn't clear though, is how often edits might go wrong and how dangerous these unwanted changes could be."Everybody in the field is watching carefully to see whether there are going to be unanticipated problems that may set the field back a bit," says Dana Carroll, a pioneer in genome editing technologies at the University of Utah.

"It's hard to predict what is going to turn up, but so far things look promising. People are forging ahead and until we run into problems that cause us to stand back and rethink, it seems like things are on a good track."

Genome editing and more conventional gene therapies might arrive in clinics as treatments for diseases that have already taken hold, but in time, some scientists expect to see gene-based treatments that make our healthy bodies more resilient to disease, or simply better than the everyday human.

George Church, director of the Centre for Computational Genetics at Harvard Medical School, points out that scientists have identified rare mutations that can boost muscle development and make stronger bones. These might make our bodies tougher and more resilient to the natural wasting that makes us more feeble and fragile with age.

Genetic modifications that enhance our natural biology could ultimately prolong our lives and save health services vast sums of money. Rare variations in a gene called PCSK9 are known to have a dramatic effect on levels of "bad" cholesterol, a major risk factor for heart disease. For some people with advantageous genetic mutations their risk of developing coronary heart disease is between half and 90% that of the general population. Were it possible, and desirable, to add these genetic mutations to the wider population, the impact on public health might be huge.

As science progresses, Church believes gene therapies and other medical technologies will be used across a "spectrum of need", from treating serious illnesses to protecting people at risk of disease and, finally, boosting the minds and bodies of the healthy.

"A huge fraction of our pharmaceuticals are aimed at enhancing our abilities, and a huge fraction of our devices are aimed at enhancement," Church says. "We have cars to improve our ability to run, computers to improve our ability to remember, and Viagra enhances our ability to, well, not everybody who uses these drugs has dysfunction. It would be truly exceptional if we managed not to use genetics and other developments that way in the future."