Abstractions

LAST AUTHOR

Giulio Cossu has devoted the past 15 years to the search for a treatment for muscular dystrophy. On page 574, he and his colleagues reveal what they believe could be a breakthrough. Cossu, based at the San Raffaele Scientific Institute in Milan, Italy, and his team have found that a type of stem cell called a mesoangioblast, which is extracted from the aorta of embryos, could be the basis of a treatment. They show how the cells allowed golden retrievers with the crippling genetic disorder to walk and even jump again — tantalizing findings that may one day lead to a human therapy.

Why test these stem cells on dogs?

There are no models of muscular dystrophy in primates. Golden retriever animal models are the best to date, because their size and general physiology is closest to humans.

Cell therapy seemed to hold little promise for muscular dystrophy. Why did you go on?

Finding the mesoangioblast stem cell was the winning point. These stem cells can cross the membrane of blood vessels and distribute themselves evenly through the downstream muscles — something that was not possible for other stem cells such as satellite cells, which would have to be injected into every 2 millimetres of muscle in the body. That would have meant thousands of injections.

What were the most surprising results?

One of the most emotional moments I had was when I saw the severely impaired dog running again. I couldn't have anticipated it going so well. I hope that this result can be transferred to humans.

Donor stem cells from healthy dogs worked better than genetically corrected cells from the afflicted patient dog. Why?

We think it mainly has to do with the micro-dystrophin used to deliver the patient dog's cells. Dystrophin is the protein that creates an elastic scaffold able to absorb the stress during muscle contraction. Donor cells from a normal dog express a dystrophin gene that makes a complete, functional protein. As dystrophin is a large protein that does not fit into most viral vectors, we used a micro-dystrophin that encodes a small version of the same protein. It showed promise in mice, but didn't work that well in dogs.

What will it take to start human trials?

First, we'll have a longer follow-up in dogs. We'll treat them like humans, continuing the administration of an immunosuppressive agent such as cyclosporine to avoid rejection of the foreign cells. Once we get the money and decide on a strategy, it will be about three years before human clinical trials. ■

MAKING THE PAPER

Jan Born

How electrical oscillations during sleep help us to remember things.

Few doubt the benefits of a good night's sleep — and research has long suggested that it helps our memories to consolidate recently learned facts. On page 610, Jan Born and his colleagues at the University of Lübeck in Germany provide fresh insight into how this consolidation process works.

Born and his team focused on the idea that electrical activity might play a role in our memories. Oscillations in electrical activity occur at different rates depending on the phase of the sleep cycle: they are at their peak during rapid-eye-movement (REM) sleep and are at their slowest during periods of deep sleep. "We asked whether these oscillations are critical to the consolidation of memories," says Born.

Born and his colleagues were aware that there was some kind of relationship between the hippocampus, the part of the brain associated with memorized facts, and the neocortex, where the slow electrical oscillations begin. During deep sleep, bursts of activity in the hippocampus are synchronized with the slow wave oscillations originating in the neocortex.

So Born and his team devised an experiment to test whether the electrical oscillations were affecting memory consolidation. They asked a group of medical students to memorize a list of words. They then attached electrodes to the students' scalps and allowed them to go to sleep. As the students entered phases of deep sleep, the researchers pulsed the students' neocortexes with electrical currents at the same frequency as would normally been seen during that part of the sleep cycle. "Essentially we wanted to mimic the phenomenon," Born says.

The team stimulated the brain for 5 minutes, stopped for 1 minute to record brain activity, and then stimulated the brain for another 5 minutes, during a 30-minute session, about the length of one slow-wave sleep cycle. "We used the one-minute intervals so that we could see the immediate effect of our stimulation," explains postdoc Lisa Marshall, who conducted the experiment.

The researchers found that the neocortex produced more pronounced slow wave oscillations after stimulation. "We were surprised about the size of the effect," says Born. After the students woke up, those who had been 'stimulated' could remember more words than the those who had not had the treatment.

Born speculates that the slow wave oscillations are transmitted to neurons in the hippocampus, causing the cells to synchronize their firing. The resulting rhythmic activity may then provide a mechanism to relay 'quanta' of information back to the neocortex during memory consolidation. The stronger the oscillations, the better the communication between these two parts of the brain, and the more memory consolidation.

As tempting as it may sound, Born warns that students should not try the experiment at home. "We did this study to show that the slow wave oscillations are relevant to memory. Medical students have lots of slow wave oscillations of their own, which are sufficient to remember things." ■

KEY CONTACTS

In many economic and geographic systems, the way we rank and order things — such as income distribution, or population number — is abstract and transitory. Michael Batty, director of the Centre for Advanced Spatial Analysis at University College London, has constructed a visual model, called a rank clock to track the rise and fall of cities and civilizations over time (see page 592).

Batty's interest in urban dynamics dates to the 1960s, when he studied architecture. But it was rekindled three years ago when he visited colleagues at Ann Arbor who were interested in the laws of rank-size distribution, which look at how amounts of resources, people and products help determine a city's composition. Batty subsequently examined data for US cities. His former PhD student, Naru Shiode, now at the State University of New York in Buffalo, suggested that what was needed was a new method of visualization.

But the final push for Batty came from learning about Doug White's work at the University of California, Irvine. White was working on the very-long-term dynamics of cities. When examining these data with rank clocks, Batty found an "amazing volatility" over a 2,500-year period, a pattern that conventional models failed to replicate, and that his model takes into account. ■