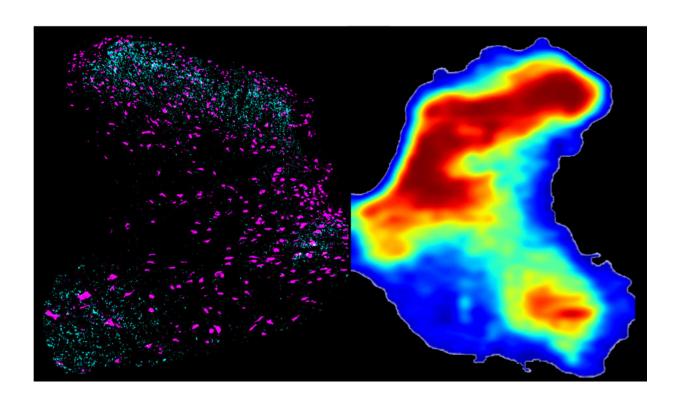


## Gene therapy restores hand function after spinal cord injury in rats

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Active neural connections in rat spinal cord. Credit: King's College London

Researchers at King's College London have shown that rats with spinal cord injuries can re-learn skilled hand movements after being treated with a gene therapy.

People with spinal cord injury often lose the ability to perform everyday



actions that require coordinated hand movements, such as writing, holding a toothbrush or picking up a drink. Regaining hand function is the top priority for patients and would dramatically improve independence and quality of life. No regenerative treatments are currently available.

The researchers tested a new gene therapy for regenerating damaged tissue in the spinal cord that could be switched on and off using a common antibiotic.

Professor Elizabeth Bradbury from the Institute of Psychiatry, Psychology & Neuroscience (IoPPN) said: "What is exciting about our approach is that we can precisely control how long the therapy is delivered by using a gene 'switch." This means we can hone in on the optimal amount of time needed for recovery. Gene therapy provides a way of treating large areas of the spinal cord with only one injection, and with the switch we can now turn the gene off when it is no longer needed."

After a traumatic spinal injury, dense scar tissue forms which prevents new connections being made between nerve cells. The gene therapy causes cells to produce an enzyme called chondroitinase which can break down the scar tissue and allow networks of nerve cells to regenerate.

Most human <u>spinal cord injuries</u> occur at the neck level and affect all four limbs. The researchers gave the gene therapy to rats with spinal injuries that closely mimicked the kind of human spinal injuries that occur after traumatic impacts such as car crashes or falls.

Dr. Emily Burnside from the IoPPN explains: "Rats and humans use a similar sequence of coordinated movements when reaching and grasping for objects. We found that when the gene therapy was switched on for two months the rats were able to accurately reach and grasp sugar pellets.



We also found a dramatic increase in activity in the spinal cord of the rats, suggesting that new connections had been made in the networks of nerve cells."

The researchers had to overcome a problem with the immune system recognising and removing the gene switch mechanism. To get around this, the researchers worked with colleagues in the Netherlands to add a 'stealth gene' which hides the gene switch from the immune system.

Professor Joost Verhaagen at the Netherlands Institute for Neuroscience says: "The use of a stealth gene switch provides an important safeguard and is an encouraging step toward an effective gene therapy for spinal cord injury. This is the first time a gene therapy with a stealth on/off switch has been shown to work in animals."

The gene therapy is not yet ready for human trials. While the ability to switch a therapeutic gene off provides a safeguard, the researchers found a small amount of the gene remained active even when switched off. They are now working on shutting the gene down completely and moving towards trials in larger species.

More information: Brain (2018). DOI: 10.1093/brain/awy158

## Provided by King's College London

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