Researchers restore coordinated limb movement in dogs with severe spinal cord injury

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(Medical Xpress)—In a collaboration between the University's Veterinary School and MRC's Regenerative Medicine Centre, scientists used a unique type of cell to regenerate the damaged part of the dogs' spines. The researchers are cautiously optimistic that the work could have a future role in the treatment of human patients with similar injuries if used alongside other treatments.

Scientists have been aware for over a decade that olfactory ensheathing cells (OEC) might be useful in treating the damaged spinal cord because of their unique properties. The cells have the ability to support nerve fibre growth that maintains a pathway between the nose and the brain.

Previous research using laboratory animals has already revealed that OECs can aid regeneration of the parts of nerve cells that transmit signals (axons) so as to form a 'bridge' between damaged and undamaged spinal cord tissue. A Phase 1 trial in human patients with SCI established that the procedure is safe.

The study, published in the latest issue of the neurology journal *Brain*, is the first double-blinded randomised controlled trial to test the effectiveness of these transplants to improve function in 'real-life' spinal cord injury. The trial was performed on animals that had spontaneous and accidental injury rather than in the controlled environment of a laboratory, and some time after the injury occurred. This far more

closely resembles the way in which the procedure might be used in human patients.

The 34 pet dogs had all suffered severe spinal cord injury. Twelve months or more after the injury, they were unable to use their back legs to walk and unable to feel pain in their hindquarters. Many of the dogs were dachshunds which are particularly prone to this type of injury. Dogs are also more likely to suffer from SCIs because the spinal cord may be damaged as a result of what in humans is the relatively minor condition of a slipped disc.

In the study, funded by the MRC, one group of dogs had olfactory ensheathing cells from the lining of their own nose injected into the injury site. The other group of dogs was injected with just the liquid in which the cells were transplanted. Neither the researchers nor the owners (nor the dogs!) knew which injection they were receiving.

The dogs were observed for adverse reactions for 24 hours before being returned to their owners. From then on, they were tested at one month intervals for neurological function and to have their gait analysed on a treadmill while being supported in a harness. In particular, the researchers analysed the dogs' ability to co-ordinate movement of their front and back limbs.

The group of dogs that had received the OEC injection showed considerable improvement that was not seen in the other group. These animals moved previously paralysed hind limbs and co-ordinated the movement with their front legs. This means that in these dogs neuronal messages were being conducted across the previously damaged part of the spinal cord. However, the researchers established that the new nerve connections accounting for this recovery were occurring over short distances within the spinal cord and not over the longer distances required to connect the brain with the spinal cord.

Professor Robin Franklin, a co-author of the study from the Wellcome Trust-MRC Cambridge Stem Cell Institute, University of Cambridge, said: "Our findings are extremely exciting because they show for the first time that transplanting these types of cell into a severely damaged spinal cord can bring about significant improvement. We're confident that the technique might be able to restore at least a small amount of movement in human patients with spinal cord injuries but that's a long way from saying they might be able to regain all lost function. It's more likely that this procedure might one day be used as part of a combination of treatments, alongside drug and physical therapies, for example."

Dr Rob Buckle, Head of Regenerative Medicine at the MRC, commented: "This proof of concept study on pet dogs with the type of injury sustained by human spinal patients is tremendously important and an excellent basis for further research in an area where options for treatment are extremely limited. It's a great example of collaboration between veterinary and regenerative medicine researchers that has had an excellent outcome for the pet participants and potentially for human patients."

The researchers stress that human patients with a spinal injury rate a return in sexual function and continence far higher than improved mobility. Some of the dogs in the study did regain bowel and bladder control but the number of these was not statistically significant.

Mrs May Hay, owner of Jasper who took part in the trail (and can be seen in the video), said: "Before the trial, Jasper was unable to walk at all. When we took him out we used a sling for his back legs so that he could exercise the front ones. It was heartbreaking. But now we can't stop him whizzing round the house and he can even keep up with the two other dogs we own. It's utterly magic."