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News roundup

Dissolving sugar helps nerve regeneration

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Nerve regeneration after brain or spinal cord injury can be improved by dissolving the sugar chains found on the inhibitory protein molecules that fill the scar tissue. Neuroscientists at the Brain Repair Centre in Cambridge have discovered that by using a bacterial enzyme to dissolve the sugar they can significantly improve the regeneration of neurones (*Nature Neuroscience* 2001;4:465-6).

One of the reasons that neurones do not grow back after an acute injury is that the glial cell scar tissue becomes full of inhibitory molecules called chondroitin sulphate proteoglycans. These proteins, which are modified by the addition of sulphated sugar chains, prevent neurones growing back through the damaged area. Knowing that the sugar chains confer most of the inhibitory properties of these molecules, Dr James Fawcett and his team of neuroscientists in Cambridge have been looking at ways to chemically remove them.

Using a rat model of brain damage, the scientists investigated whether a bacterial enzyme called chondroitinase ABC would dissolve the sugar chains. They inflicted damage on the nigrostriatal system (the part of the brain damaged in Parkinson's disease) and observed that the resulting scar tissue was accompanied by an increase in the amount of chondroitin sulphate proteoglycans at the site of the injury. They then infused chondroitinase ABC into the injured area and found that within a week the damaged axons that produce dopamine had regrown by up to 1 cm in length towards their original target, with evidence of axon terminals actually in the striatum itself. No regrowth of neurones was seen in the control rats.

Having shown that chondroitinase treatment promotes regeneration in this simple axon pathway, Dr Fawcett's team started a collaboration with Dr Elizabeth Bradbury at King's College London to see whether chondroitinase ABC also works when applied to spinal cord injuries. In these experiments the damaged axons regrew to a length of 2 cm, and there was functional improvement (*Society for Neuroscience Abstracts* 2000;26:860).

Chondroitinase ABC was chosen because of its ability to selectively digest chondroitin sulphate molecules—not heparin sulphate molecules, which are also found at the site of injuries and are known to promote tissue repair. The main limitation of long term enzyme infusion is that it induces an immune response. "We see this enzyme as potentially useful in the acute phase of a brain injury, but it would have to be followed by treatments which work in other ways," explained Dr Fawcett. One option would be to dissolve the sugar with chondroitinase ABC and then add something else that blocks further proteoglycan synthesis. Ultimately, the successful treatment of spinal cord injuries is likely to require a cocktail of enzymes and nerve growth factors.