Systemic delivery of a mimetic peptide against connexin43 gap junction protein in rats following spinal cord injury

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A major challenge in the management of spinal cord injury is development of an effective treatment that can be delivered to patients in a timely manner after a traumatic accident. A mimetic peptide, Peptide5 (P5), against the gap junction protein connexin43 has been shown previously to reduce tissue damage and improve functional outcomes when delivered directly to the lesion site in a rat model of spinal cord injury. In this study we asked whether acute systemic delivery of peptide5 is protective. Intraperitoneal injections of mimetic peptide (P5) or scrambled peptide (SP) were given immediately after a mild contusion injury in rats using the NYU impactor model, with injections repeated at 2 and 4 hours post-injury. Rats were euthanised at 8 hrs (n=8) or 2 weeks (n=32) post injury. Immunohistochemistry was performed on longitudinal tissue samples. Results show that P5 treatment reduced Cx43 protein and increased phosphorylated Cx43 protein 8 hrs after injury compared to SP ($p < 0.05$). At 2 weeks a reduction in lesion size, and the astrocytic (GFAP), macrophage (ED1) and microglial (IBA1) response was seen ($p < 0.05$). In addition, neuronal (NeuN) numbers were higher in the P5 treated animals compared to the SP rats ($p < 0.05$). These results suggest that Peptide5, administered systemically, has a positive effect in ameliorating the effects of spinal cord injury. The effects of Peptide5 treatment at later time points and on improvement in functional outcomes over time will be further investigated.