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Sulfonylureas—a novel treatment to reduce tissue damage after acute spinal cord injury?

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The December issue of *The Lancet Neurology* features a Review article by Ramer and colleagues,¹ which gives an excellent overview of best practices and promising new research directions for treatment of spinal cord injury (SCI). We would like to add the following new angle on this crucial matter: the sulfonylurea receptor 1–transient receptor potential melastatin 4 (SUR1–TRPM4) channel is upregulated within hours of SCI at the site of the lesion.² After CNS injury, the SUR1–TRPM4 channel has been detected in neurons, astrocytes, oligodendrocytes, and microvascular endothelium at the site of injury. Increased expression of this cation channel has been linked to development of vasogenic and cytotoxic oedema, and to subsequent hemorrhagic conversion.^{2,3} Glibenclamide is an antidiabetic agent from the class of sulfonylureas that acts as an inhibitor of SUR1. Accumulating evidence indicates that glibenclamide might exert beneficial effects in various CNS pathologies.² Some of these effects of glibenclamide might relate to protection of microvascular endothelium, reduced oedema formation, secondary hemorrhage, and anti-apoptotic and anti-inflammatory mechanisms.² Importantly, penetration of glibenclamide into the CNS is enabled after focal injury.²

Ramer and colleagues reference a promising recent phase I trial⁴ of riluzole in acute SCI. It is worth mentioning that, among other effects, riluzole blocks TRPM4. Furthermore, results of a study of severe spinal cord injury in rats showed superiority of glibenclamide over the glutamatergic neurotransmission blocker riluzole regarding complex motor functions, tissue sparing at 6 weeks, and toxicity.⁵ Clearly, the SUR1–TRPM4 channel deserves further investigation as a drug target in SCI.

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