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Improving functional recovery after severe spinal cord injury by a noninvasive dual functional approach of neuroprotection and neuromodulation.

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Despite tremendous unmet medical needs, there is no effective pharmacological treatment to promote functional recovery after spinal cord injury (SCI). Although multiple pathological events have been implicated in SCI, the development of a noninvasive pharmacological approach to simultaneously target the different mechanisms involved in SCI remains a formidable challenge. In this study, we report the development of a noninvasive nanodrug delivery system that consists of ROS-responsive amphiphilic copolymers and an encapsulated neurotransmitter-conjugated KCC2 agonist1,2. We show that upon intravenous administration, the nanodrugs were able to enter the injured spinal cord due to blood spinal cord barrier disruption and ROS-responsive disassembly. Remarkably, once in the injured spinal cord, these nanodrugs exhibited dual functions: scavenging ROS accumulated in the lesion to protect spared connections and increasing neuronal excitability in the injured spinal cord through targeted delivery of the KCC2 agonist to inhibitory neurons. Thus, the noninvasive treatment led to significant functional recovery in the rats with contusive SCI3. Together, these findings provide a much-needed translational pharmacological approach for treating severe SCI