Studies in experimental animal models have demonstrated that the mammalian spinal cord can generate rhythmic or tonic motor output even in the absence of input from the brain. This evidence led to the hypothesis that if similar spinal circuits exist in humans, then electrically stimulating the lumbosacral spinal cord in combination with motor activity could facilitate motor function and mobility in patients with spinal cord injury (SCI). In a seminal case study by Harkema et al. in 2011, an adult with chronic motor complete paraplegia underwent epidural spinal stimulation therapy, could maintain minimally assisted standing, and revealed significant levels of voluntary control of the lower limbs during stimulation. Later, these outcomes were expanded in studies performed by the research teams at Mayo Clinic and of Dr. Courtine. Similar functional outcomes can be obtained using transcutaneous spinal stimulation, demonstrating the feasibility of a non-invasive approach to facilitate motor functions and neuromodulate excitability at multiple levels of the spinal neuraxis, ranging from the cervical to the coccygeal cord levels. Activation of sub-functional longitudinal fibers across the lesion, and emerging responsiveness of spinal networks below the lesion to descending commands and proprioception is considered the main mechanism for both invasive and non-invasive spinal stimulation to restore function after paralysis. Yet, we still have a lack of understanding on the type and characteristics of interventions and the dose-response effects, to promote a given function. In addition, we have limited knowledge on the extent to which motor and autonomic functions can be restored, when/if the restored function can become independent of the used intervention, and which clinical populations can benefit from spinal neuromodulation.