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Factors that affect the degree of axonal regeneration following spinal cord transection in larval lamprey

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In all vertebrate animals, reticulospinal (RS) neurons in a locomotor "command" systems in the brain send neural processes to the spinal cord to activate "central pattern generators" (CPGs) and initiate locomotor behavior. Unlike higher vertebrates, such as birds and mammals, lower vertebrates such as lamprey can behaviorally recover following spinal cord injury because axons from brain neurons regenerate and reconnect with neurons in the spinal CPGs. Although the lamprey can behaviorally recover following spinal cord transections, most injured axons regenerate for relatively short distances below the lesion. Thus, axonal regeneration is incomplete, possibly because regenerating axons make synapses just below the lesion, and these synapses might provide factors that suppress further regeneration. We hypothesize that following spinal cord transection, the degree to which axons of RS neurons are stimulated to regenerate is determined, in part, by the numbers of synapses these neurons have made, either above or below the lesion. Preliminary results indicate that rostral spinal cord transections are a "strong" stimulus for regeneration, while caudal spinal cord transections are a relatively "weak" stimulus. The purpose of the present study was to determine the degree to which the above "strong" or "weak" axonal regeneration could initiate locomotor activity below the lesion. Spinal cord transections were made at 10% body length (BL, normalized distance from the head; "rostral" lesion) or 50% BL ("caudal" lesion) in larval lamprey. After various recovery times, muscle activity (EMGs) was recorded below each of the two types of lesions to determine the degree of recovery of locomotor activity. First, 2 weeks after rostral spinal cord transections, animals could produce weak swimming movements, and muscle activity was present just below the lesion. With increasing recovery times muscle activity could be recorded at progressively lower levels of the body. Second, 2 weeks after caudal spinal cord transections, muscle activity was present above the lesion, but did not appear just below the lesion until ~8 weeks after the lesion. The results indicate that following rostral (caudal) spinal cord lesions, axonal regeneration from RS neurons is robust (weak), and locomotor behavior recovers relatively quickly (slowly). These results support our hypothesis and suggest that factors associated with the number of synapses are involved in controlling regeneration. Identification of these factors might be used to modulate axonal regeneration following spinal cord injury, especially in animals where regeneration is limited, such as humans.