Discussion

Motor versus Sensory Neuron Regeneration through Collagen Tubules

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Discussion by Roger D. Madison, Ph.D.

The report by Madorsky et al. examines the differential ability of rat motor and sensory neurons to regenerate an axon after transection of the sciatic nerve. Three experimental conditions are examined: conventional epineurial repair, epineurial repair enclosed by a collagen tube (cuff repair), and a 10-mm nerve gap bridged by a collagen tube. The number of motor and sensory neurons that regenerated an axon into the peroneal nerve branch was estimated by horseradish peroxidase retrograde labeling and examination of positive neurons in the spinal cord and L2 to L6 dorsal root ganglia. Not surprisingly, the conventional epineurial repair and the epineurial cuff repair displayed the greatest number of retrogradely labeled neurons. For example, in the epineurial repair, 65 percent of the normal number of motor neurons and 79 percent of the normal number of sensory neurons were labeled. In all experimental groups, the proportion of sensory neurons was higher than that for motor neurons. The authors conclude that sensory neurons display a more robust regeneration response.

These data are somewhat complicated by the fact that the nerve lesion was carried out on the common sciatic nerve, but the retrograde labeling was from just the peroneal branch of the sciatic nerve. Previous retrograde labeling studies carried out by Dr. Swett's laboratory have elegantly shown that if retrograde labeling is carried out from the common sciatic nerve, approximately 2000 motor neurons and 10,500 dorsal root ganglia neurons are labeled.[1,2] In the present study, because the repair site involved the common sciatic nerve, there is the possibility that any of these lesioned neurons could send an axon into the peroneal branch during regeneration, and, thus, become retrogradely labeled. The data in Table I can be reanalyzed with this in mind. For the epineurial repair, 409 motor neurons and 2127 dorsal root ganglia neurons were labeled. These numbers represent approximately 20 percent of the total number of transected motor or sensory neurons respectively, i.e., 409 of 2000 and 2127 of 10,500. A similar analysis of the cuff repair group yields 17 percent and 18 percent of the total number of transected motor or sensory neurons, respectively. When the data are analyzed in this fashion, the proportion of regenerating sensory and motor neurons is quite similar. Thus, for the epineurial and cuff repair groups, it may be misleading to conclude that sensory neurons display a more robust regeneration response.

Conversely though, the 10-mm gap repair group supports the conclusion of more robust sensory neuron regeneration. In this group, 39 and 1710 motor and sensory neurons were labeled, respectively. These numbers represent approximately 2 percent and 16 percent of lesioned motor and sensory neurons, respectively. Sensory neurons are more successful under these adverse regeneration conditions, when a nerve gap must be bridged. Thus, this study helps to focus attention on the fact that differences exist between the ability of sensory and motor neurons to regenerate after axon transection and that such differences may be

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especially pertinent under more adverse regeneration conditions.

An additional problem highlighted by these studies is the question of specificity of regeneration. It would be extremely useful to know not just the number of motor and sensory neurons that have regenerated an axon, but also whether or not those neurons that are retrogradely labeled after regeneration originally projected an axon into that particular nerve branch. Such an analysis could identify a neuron that originally projected to the tibial branch of the sciatic nerve but has now regenerated an axon to the peroneal branch. In terms of functional recovery, it may be important to differentiate between these neurons and those that originally projected to the peroneal branch and have returned to the peroneal branch. A labeling model that allows such analysis at the individual nerve branch level has recently been described and should prove useful in studies aimed at the specificity of nerve regeneration.[3,4]

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