Heterogeneity of the Regenerative Response of Dorsal Root Ganglion Neurons to a Conditioning Lesion

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Dorsal root ganglia (DRG) are composed of different subsets of sensory neurons which are distinguished by size and function in terms of the stimuli to which they respond. Nerve injury in the peripheral nervous system causes cellular and molecular changes such as up- and downregulation of specific genes. It also causes regeneration of axons of DRG neurons in vivo and in vitro. However, peptidergic and nonpeptidergic nociceptors that express CGRP or bind to IB4 respectively have been reported to have a poor ability to regenerate compared to the remaining non-stained neurons after a conditioning lesion (Kalous and Keast, 2010). We have replicated these findings and gone on to investigate which specific groups of neurons are responsible for the conditioning lesion response among the non-stained cells. We examined neurite outgrowth by dissociated DRG neurons after sciatic nerve injury transection and stained the neurons with various cell specific markers. In addition, since CGRP staining and IB4 binding decrease after axotomy, neurons from Cre-mouse lines for promoters of CGRP and MrgD (which is expressed by IB4-binding neurons) were tested for neurite outgrowth. Seven days after unilateral axotomy, cells were harvested, dissociated into single cells, and cultured for 24 hrs. Immunocytochemistry was performed and cells were analyzed by comparing % of neurons with neurites and measuring the longest neurites per neuron. Out of various markers, TrkC+ neurons showed the biggest neurite outgrowth and elongated mode of regeneration after sciatic nerve injury. Additionally, genetically labelled CGRP- and MrgD-positive neurons showed a conditioning lesion effect after axotomy while CGRP antibody-stained and IB4-bound cells did not exhibit any change. These results indicate that certain subgroups of DRG neurons grow better than others, and genetically-labelled CGRP and MrgD may have gone through post-transcriptional or translational changes after axotomy to account for their change in outgrowth.