CNS myelin fails to downregulate GAP-43 protein expression in DRG neurons.

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CNS myelin inhibits axon growth in vivo and in vitro. Inverse patterns of myelin distribution and GAP-43 expression in normal and pathological spinal CNS suggest that inhibition of GAP-43expression may be involved in inhibition of axon growth by CNS myelin.

We have quantified the effects of CNS myelin membrane fragments on GAP-43 expression and neurite outgrowth by cultured adult rat DRG neurons. As measured by cell-ELISA, exposure to cAMP analogues, forskolin or cholera toxin for 7 d.i.v. reduces GAP-43 expression, but exposure to CNS myelin fragments for the same time period does not. Counts of DRG neurons identified by immunocytochemistry for MAP-2 indicate that the experimental treatments have no effect on neuronal survival which would influence the ELISA data. Growth potential of DRG neurons after 7 d.i.v. was measured by dislodging DRG neurons and replating them under identical experimental conditions, then measuring neurite growth after 8 hours in secondary culture. Neurons exposed to cAMP analogues, forskolin of cholera toxin exhibit increased neurite outgrowth, but neurons exposed to CNS myelin fragments exhibit a dramatic decrease in neurite outgrowth during this test period, as compared to control secondary cultures.

These results show that inhibition of growth of neurites by adult DRG neurons in vitro does not involve down-regulation of GAP-43 protein. The inhibitory effect of myelin may therefore occur only at the level of the growth cone.

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