SCHWANN CELLS MODULATE THE RELEASE OF CALCITONIN GENE-RELATED PEPTIDE FROM SENSORY NEURONS

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An alteration in the interaction between Schwann cells and sensory neurons may be involved in inflammatory neuropathies associated with altered sensation and pain. The release of the peptide transmitter, calcitonin gene-related peptide (CGRP), is one method to monitor the sensitivity of a subclass of primary sensory neurons involved in pain signaling. We utilized an *in vitro* assay to investigate the interaction between Schwann cells and sensory neurons in an inflammatory state. Schwann cells and sensory neurons were isolated from adult mouse sciatic nerve and dorsal root ganglia, respectively, and maintained in culture. Schwann cells were exposed to HEPES buffer containing the inflammatory mediators histamine, prostaglandin E_2, bradykinin, and serotonin (all 10^{-5} M), potassium (7 mM), and at pH 7.0 for 10 minutes. After this activation, the Schwann cells were incubated in HEPES buffer alone for 1 hour. This Schwann cell-conditioned buffer (SCCB) was collected and sensory neurons were exposed to three consecutive 10 minute incubations in HEPES buffer alone or SCCB. The amount of CGRP released during each of these incubations was measured using radioimmunoassay. Incubation with SCCB elicited a seven-fold increase in the release of CGRP compared to neurons exposed to HEPES buffer alone. The release of CGRP elicited by SCCB was abolished when neurons were exposed to SCCB containing no added calcium. After treatment with the inflammatory mediators detailed above for 10 minutes, Schwann cell lysates showed a significant decrease in six cytokines, while SCCB demonstrated an increase in interleukin-6 (IL-6) as measured by a cytokine array panel. These results suggest that during inflammation, Schwann cells release substances, which directly stimulate sensory neurons, as measured by an increase in CGRP release. These findings reinforce the importance of identifying the mechanisms underlying the interaction between Schwann cells and sensory neurons to discover novel therapeutics for treating inflammatory pain.