Loss of local innervation induces lymph node expansion

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Peripheral lymphoid and non-lymphoid tissues receive direct innervation via the nervous system but the relevance of neural input for the mounting of immune responses remains largely unknown. Ablating local innervation to popliteal lymph nodes (popLNs) by unilateral surgical ligation of the sciatic nerve led to footpad edema and dramatic expansion of popLNs due to an increase in cellularity in the ipsilateral side. In contrast, local surgeries leaving popLNs innervated, such as femoral denervation or sciatic denervation downstream of the popliteal fossa, did not generate nodal expansion. The increase in lymph node cellularity could be attributed to B cell proliferation and was associated with enhanced lymphocyte homing from the blood while leukocyte egress from effenter lymph remained unchanged. Homing was a critical factor in this process since blocking leukocyte entry into the lymph node with antibodies directed against L-selectin or both α4- and αL-integrins ablated denervation-induced nodal expansion. Higher levels of TNF-α, IL-17 and IL-4 were detected in denervated lymph nodes, the latter of which was also observed by systemic or local sympathectomy. Thus, loss of neural input to lymph nodes resulted in increased cellularity which was dependent on leukocyte homing. These data provide evidence for an important role of direct neural innervation in the control of immune responses.

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