Local sympathetic neurons promote neutrophil egress from the bone marrow at the onset of acute inflammation

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The sympathetic nervous system plays critical roles in the differentiation, maturation, and recruitment of immune cells under homeostatic conditions, and in responses to environmental stimuli, although its role in the migratory control of immune cells remains unclear. In this study, using an advanced intravital bone imaging system, we demonstrated that the sympathetic nervous system locally regulates neutrophil egress from bone marrow for mobilization to inflammatory foci. We found that sympathetic neurons were located close to blood vessels in the bone marrow cavity; moreover, upon lipopolysaccharide (LPS) administration, local sympathectomy decreased the velocity of neutrophils, and increased the proportion of neutrophils that remained in place. We also showed that vascular endothelial cells produced C-X-C motif chemokine ligand 1 (CXCL1), which is responsible for neutrophil egress out of bone marrow. Its expression was upregulated, and was suppressed by β-adrenergic receptor blockade, resulting in inhibition of neutrophil egress into the systemic circulation. Furthermore, systemic β-adrenergic signaling blockade decreased the recruitment of neutrophils in the lung under acute systemic inflammation. Taken together, the results of this study demonstrated a new regulatory system, wherein local sympathetic nervous activation promoted neutrophil egress by inhibiting *Cxcl1* expression in bone marrow endothelial cells in a β-adrenergic signaling-dependent manner, contributing to the recruitment of neutrophils at the onset of inflammation.