

## Splenic 6-hydroxydopamine injection exacerbates renal injury in a murine model of lupus

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Recent studies suggest that the splenic nerve regulates inflammation through the *cholinergic anti-inflammatory pathway (CAP)*. Activation of this pathway through the efferent vagus nerve causes the release of norepinephrine from the splenic nerve. Once norepinephrine binds its receptors on acetylcholine-producing T cells in the spleen, it halts the production and secretion of splenic pro-inflammatory cytokines. We have demonstrated that pharmacological stimulation of the CAP reduces pro-inflammatory mediators in a mouse model of systemic lupus erythematosus (SLE), an autoimmune disease that predominantly affects women. In the current experiment, we set out to determine whether blocking neurotransmission in the CAP would worsen inflammation. We hypothesized that depletion of splenic norepinephrine would exacerbate inflammatory responses and tissue injury in SLE mice. To test this, we injected the neurotoxin 6-hydroxydopamine (6-OHDA) or saline directly into the spleen of anesthetized female control (*NZW*) and lupus (*NZBWF1*) mice at 33 weeks of age. Two weeks following 6-OHDA injection, the animals were euthanized and tissues harvested. Splenic TNF showed no differences amongst SLE groups; however, the increased albuminuria, an index of renal injury, in SLE mice compared to controls ( $228.5 \pm 78.9$  vs.  $5.4 \pm 5.4$   $\mu\text{g}/\text{mL}$ ) was further exaggerated by 6-OHDA in SLE mice ( $9513.8 \pm 6203.4$ ; all  $p < 0.05$ ). Although it seems depletion of splenic norepinephrine does indeed worsen renal outcome in SLE, several pieces of data are required before the importance of splenic norepinephrine in subduing aberrant inflammatory responses via the CAP in SLE is apparent. *Studies funded by the American Heart Association (14SDG18320033).*