

# Chronic Low-Level Vagus Nerve Stimulation Reduces Stellate Ganglion Nerve Activity and Paroxysmal Atrial Tachyarrhythmias in Ambulatory Canines

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## Abstract

**Introduction:** Left sided low-level vagus nerve stimulation (LL-VNS) is used clinically for epilepsy and depression. We hypothesize that LL-VNS can suppress sympathetic outflow and reduce atrial tachyarrhythmias in ambulatory dogs.

**Methods:** We implanted in 12 dogs a neurostimulator in left cervical vagus nerve and a radiotransmitter for continuous recording of left stellate ganglion nerve activities (SGNA), left thoracic vagal nerve activities (VNA) and electrocardiograms. The first 6 dogs (Group 1) underwent 1 week continuous LL-VNS. Another 6 dogs (Group 2) underwent intermittent rapid atrial pacing followed by active or sham LL-VNS on alternate weeks.

**Results:** Integrated SGNA was significantly reduced during LL-VNS ( $7.8 \pm 0.9$  mV-s vs.  $9.4 \pm 0.9$  mV-s at baseline,  $P < 0.05$ ) in Group 1. The reduction was most apparent from 7 to 9 AM, (31% reduction,  $10.8 \pm 2.5$  mV-s versus  $15.6 \pm 2.9$  mV-s at baseline,  $P < 0.01$ ), along with a significantly reduced heart rate ( $P < 0.05$ ). SGNA-induced heart rate acceleration averaged  $107.9 \pm 9.0$  bpm during LL-VNS and  $129.2 \pm 9.3$  bpm at baseline ( $P < 0.05$ ). LL-VNS did not change VNA. The tyrosine hydroxylase-positive nerve structures in the left stellate ganglion were  $99,684 \pm 22,257$   $\mu\text{m}^2/\text{mm}^2$  in LL-VNS dogs and  $186,561 \pm 11,383$   $\mu\text{m}^2/\text{mm}^2$  ( $P < 0.01$ ) in normal control dogs. In Group 2, the frequencies of paroxysmal atrial fibrillation and atrial tachycardia during active LL-VNS were  $1.4 \pm 2.5/\text{d}$  and  $8.0 \pm 5.8/\text{d}$ , respectively, significantly lower than during sham stimulation ( $9.2 \pm 6.2/\text{d}$ ,  $P < 0.01$  and  $22.0 \pm 4.4/\text{d}$ ,  $P < 0.001$ , respectively).

**Conclusion:** LL-VNS suppresses SGNA and reduces the incidences of paroxysmal atrial tachyarrhythmias in ambulatory dogs. Significant neural remodeling of the left stellate ganglion is evident one week after cessation of chronic LL-VNS.