SUPPLEMENTAL MATERIAL

Region specific parasympathetic nerve remodeling in the left atrium contributes to creation of a vulnerable substrate for atrial fibrillation.

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Supplemental figures

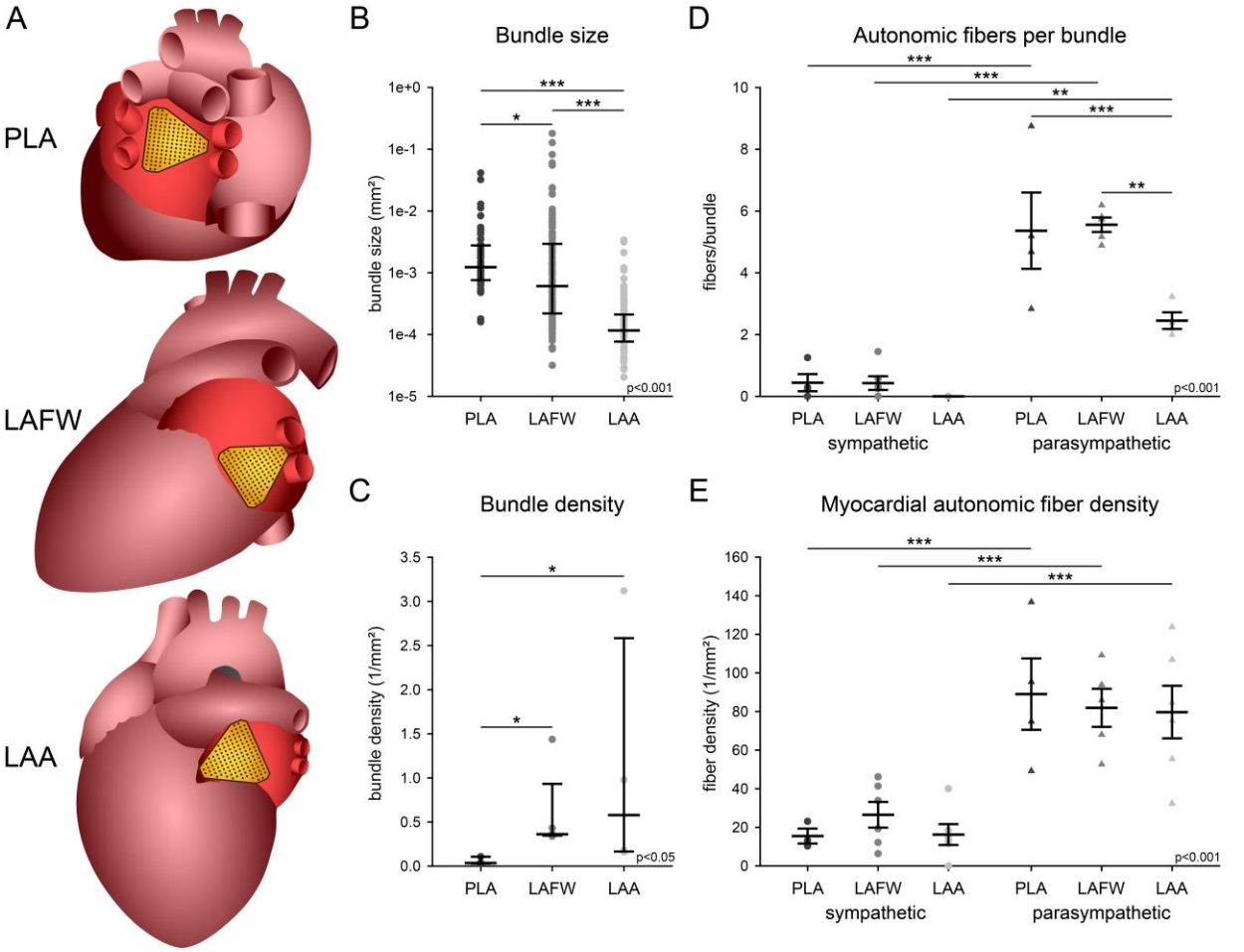

Figure S1. Autonomic innervation of the canine left atrium. **(A)** Schematic representation of the three studied regions of the left atrium: the posterior left atrium (PLA), left atrial free wall (LAFW) and left atrial appendage (LAA). A high-density electrode is represented at the regions of interest. **(B)** Combined nerve bundle size in the PLA, LAFW and LAA is shown as median with interquartile range. n=53 and N=4 for PLA, n=138 and n=6 for LAFW, and n=112 and N=5 for LAA. **(C)** Nerve bundle density in the PLA, LAFW and LAA is shown as median with interquartile range. N=3 for PLA, N=5 for LAFW, and N=4 for LAA. **(D)** Autonomic fiber content in left atrial bundles is shown as mean ± SEM for sympathetic and parasympathetic fibers in the PLA, LAFW and LAA. For sympathetic fibers, N=4, 6 and 5 respectively and for parasympathetic fibers, N=4, 5 and 4. **(E)** Myocardial autonomic fiber density in the left atrium is shown as mean ± SEM for sympathetic and parasympathetic fibers in the PLA, LAFW and LAA. For sympathetic fibers, N=3, 6 and 6 respectively and for parasympathetic fibers, N=4, 5 and 6. One or two way ANOVA significance indicated in graphs. For values that remained non-parametric despite transformation, Kruskal-Wallis one way ANOVA on ranks was performed. * P<0.05, ** p<0.01, *** p<0.001 for pairwise comparison with Holm-Sidak or Dunn's method.

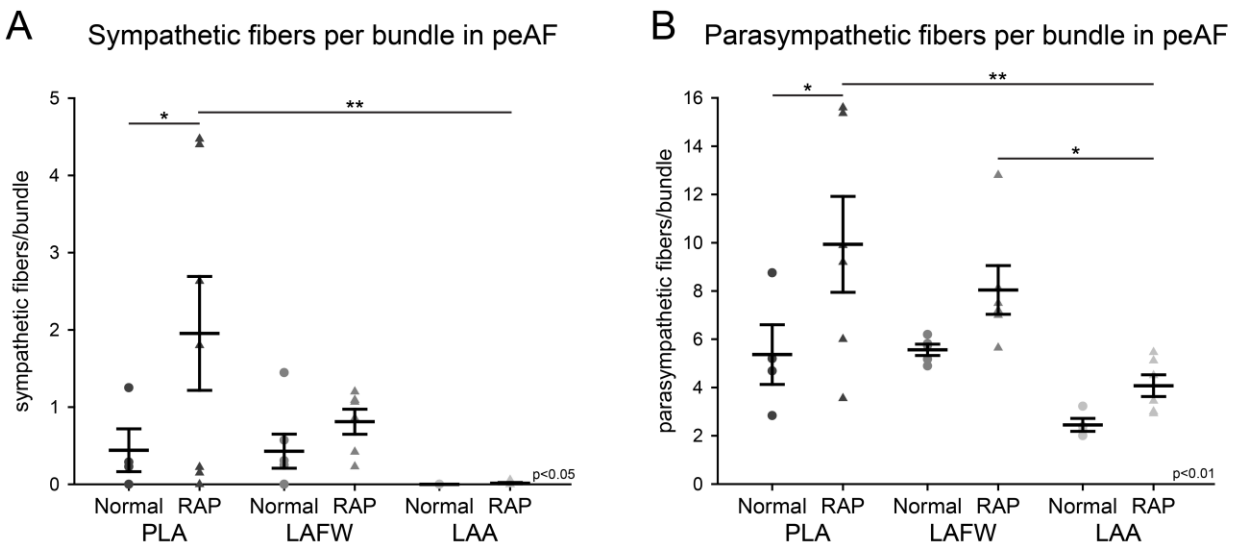

Figure S2. Autonomic fiber composition of atrial nerve bundles. **(A)** Number of sympathetic fibers in nerve bundles in the PLA, LAFW and LAA of normal dogs or after RAP is shown as mean ± SEM. N=4, 7, 6, 6, 5 and 6, respectively. **(B)** Number of parasympathetic fibers in nerve bundles in the PLA, LAFW and LAA of normal dogs or after RAP is shown as mean ± SEM. N=4, 6, 5, 6, 4 and 6, respectively. Two way ANOVA significance indicated in graphs. * $p<0.05$, ** $p<0.01$ for pairwise comparison with Holm-Sidak method.

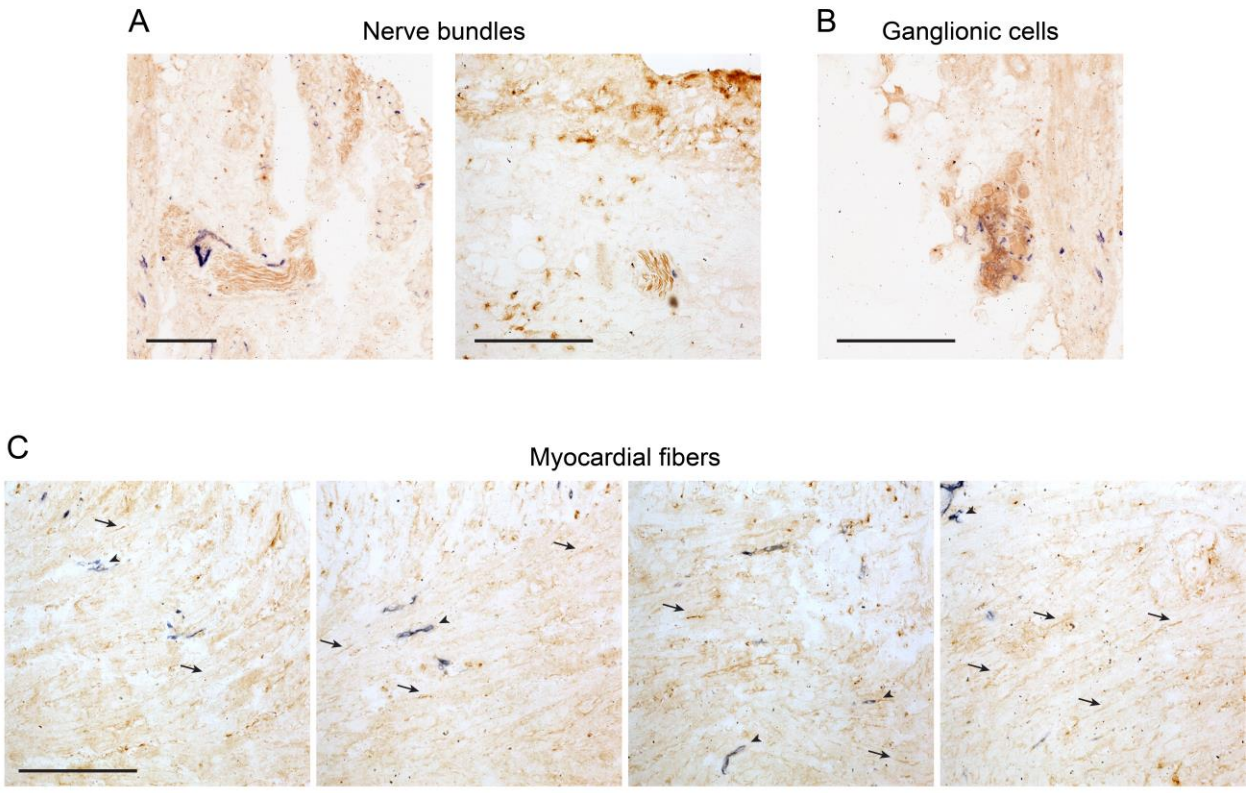

Figure S3. Autonomic innervation in the rapidly paced right atrium is comparable to the left atrium. **(A)** Representative micrographs of immunohistochemistry for AChE (brown) and DBH (blue) on right atrial tissue showing nerve bundles, ganglionic cells **(B)** and myocardial fibers **(C)** after rapid atrial pacing. Examples of parasympathetic (AChE positive) fibers indicated with arrows. Examples of sympathetic (DBH positive) fibers indicated with arrowheads. Scale bars = 200μm.

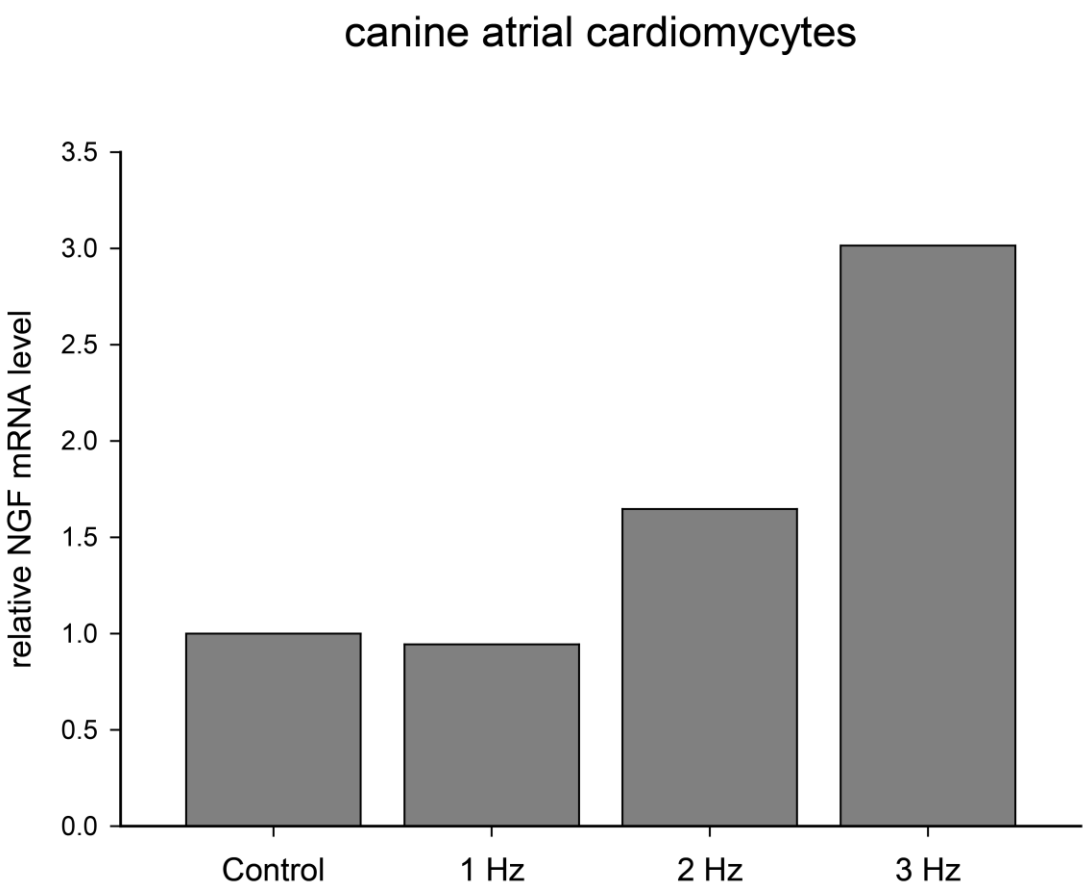

Figure S4. NGF secretion by primary atrial myocytes is dependent on frequency of activation. Relative NGF mRNA level in isolated canine atrial myocytes in control conditions or after pacing at 1 Hz, 2 Hz or 3 Hz. N=1, PCR performed in duplicate.