GW27-e1113

TNF-α increases ganglionated plexi activity and promotes atrial fibrillation in a canine model

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OBJECTIVES Clinical evidence have shown that atrial fibrillation (AF) patients are associated with increased level of TNF-α. This study aimed to investigate the effects of TNF-α microinjection on the ganglionated plexi activity and on the AF inducibility.

METHODS In fourteen anaesthetised open-chest dogs, 0.5 ml TNF-α (5ug/ml) (Group 1, n=8) or saline (Group 2, n=6) was microinjected into anterior right ganglionated plexi (ARGP). At baseline and 30 min after TNF-α or saline microinjection, 40 ms of high frequency stimulation was delivered 2 ms after atrial pacing to determine the AF threshold at each atrial and pulmonary vein (PV) site. ARGP neural activity and ARGP function (determined by heart rate reduction in response to ARGP stimulation) were also measured before and after the microinjection. C-fos protein expressed in the ARGP was examined in 2 groups at the end of study.

RESULTS In Group 1, when compared to baseline, microinjection of TNF-α significantly: (1) decreased AF threshold in all sites; (2) enhanced the sinus rate slowing response induced by ARGP stimulation; (3) increased the frequency and amplitude of the neural activity recorded from ARGP. However, in Group 2, there is no significant difference in these parameters before and after saline microinjection. In addition, the expression of c-fos protein was significantly higher in Group 1 than Group 2.

CONCLUSIONS Microinjection of TNF-α into ARGP increases AF inducibility, probably by enhancing the neural activity of ARGP.

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IL-1β aggravates ventricular arrhythmia through increasing the activity of the left stellate ganglion in an acute ischemia canine model

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OBJECTIVES Previous studies demonstrated that increased inflammation was associated with the incidence and severity of ventricular arrhythmias (VAs) and left stellate ganglion (LSG) hyperactivity promotes VAs. The present study aimed to investigate whether exogenous recombinant IL-1β could aggravate VAs through increasing the activity of the LSG.

METHODS Eighteen canines were averagely and randomly divided into IL-1β group and saline group. A final volume of 0.1ml IL-1β (5μg/ml) or saline was microinjected into the LSG. Ventricular effective refractory period (ERP), action potential duration (APD), LSG function defined as the relative change of maximal systolic blood pressure (SBP) in response to direct LSG electrical stimulation (20Hz, 0.1 ms pulse width), and LSG neural activity were measured at baseline, 10 min after the injection and 60 min after acute ischemia. Acute ischemia was induced through occlusion of left anterior descending branch (LAD) and VAs were recorded for 60 min. The LSG tissue samples were collected to evaluate the expression of NGF and c-fos.

RESULTS Ventricular ERP and APD90 were significantly decreased by IL-1β when compared with saline group. Also, increased LSG function and LSG spontaneous neuron activity were observed in IL-1β group under normal condition. More importantly, increased LSG neural activity induced by ischemia in the saline group was further aggravated by IL-1β and VAs were significantly increased in the IL-1β group. The expression of NGF and c-fos, which promoting the pathological neural remodeling of LSG, was up-regulated by IL-1β.

CONCLUSIONS IL-1β aggravates VAs induced by acute ischemia, possibly through the over-activation of the LSG.

GW27-e1115

E23K variant of the Kir6.2 subunit of KATP channel increases the susceptibility of ventricular arrhythmia in response to ischemia in rats

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OBJECTIVES Previous studies indicated that E23K variant of the Kir6.2 subunit of ATP sensitive potassium (KATP) channel was implicated in cardiac remodeling. The present study aimed to evaluate the effects of E23K variant on ventricular electrophysiology and arrhythmogenesis.

METHODS Transgenic rats were generated to express human wild type or E23K variant genomic DNA in the heart under α-myosin heavy chain promoter. Electrophysiological parameters including electrocardiograph, ventricular action potential duration (APD), and effective refractory period (ERP) were recorded at baseline and 30 min after acute ischemia. Acute ischemia was induced through occlusion of left anterior descending branch (LAD).

RESULTS No difference was found for electrophysiological parameters between wild type and E23K variant rats at baseline. However, after acute ischemia stress, shortened QT intervals were further aggravated in E23K variant rats. Also, E23K variant exacerbated the decrease of APD70, APD90 and ERP. Ventricular arrhythmia and alternant threshold was significantly decreased, and duration of ventricular arrhythmia induced by electrical stimulation was significantly prolonged in E23K variant rats.

CONCLUSIONS E23K variant of the KATP channel increased the susceptibility of ventricular arrhythmia induced by acute ischemia.

GW27-e1116

Noninvasive vagus nerve stimulation prevents catecholamine-induced ventricular tachycardia through autonomic modulation in a canine model

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OBJECTIVES Catecholamines can result in ventricular tachyarrhythmias. We examined whether noninvasive vagus nerve stimulation (NVNS) can prevent epinephrine-induced ventricular tachycardia (VT) in a canine model.

METHODS Fourteen open-chest anesthetized dogs were randomly designed into NVNS group (NVNS plus epinephrine injection, n=7) and control group (sham stimulation plus epinephrine injection, n=7). NVNS was performed for 1 hour before the administration of epinephrine. T-wave alternans (TWA) level, VT prevalence, the VT threshold (according to the dose of epinephrine administered), left stellate ganglion (LSG) function and neural activity were compared between the two groups.

RESULTS Compared to baseline, NVNS for 1 hour significantly attenuated LSG function and neural activity, whereas no significant change was shown after 1 hour of sham stimulation. Injection of epinephrine resulted in a significant increase in TWA level and LSG neural activity in the control group, which were attenuated in the NVNS group. NVNS dramatically decreased VT prevalence and increased VT threshold when compared to the control group. In addition, NVNS eliminated the VT-associated hypotension.

CONCLUSIONS NVNS could prevent catecholamine-induced VT, possibly by suppressing LSG activity.

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Left cardiac sympathetic denervation with neuron targeted nanoparticles improves cardiac function and reduces ventricular arrhythmia inducibility in a canine post-infarction heart failure model

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