Letter to the Editor

A potential link between left stellate ganglion and renal sympathetic nerve: An important mechanism for cardiac arrhythmias?

Bing Huang, Lilei Yu, Hong Jiang *

Department of Cardiology, Renmin Hospital of Wuhan University, Cardiovascular Research Institute of Wuhan University, Wuhan, China

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Atrial fibrillation is the most common arrhythmia in clinical practice, and ventricular arrhythmias represent the major mechanism of sudden cardiac death which is the leading cause of death in United States. It is now well established that the autonomic nervous system has an important role in the genesis and maintenance of these cardiac arrhythmias [1]. Therefore, modulating autonomic activity has been proposed as a method to potentially suppress cardiac arrhythmias.

Increased nerve activity of left stellate ganglion (LSG) has been shown to contribute to the generation of cardiac arrhythmias. In a canine model of atrial pacing-induced atrial fibrillation, Tan et al. found that simultaneous sympathovagal discharges (recording from LSG and left vagal nerve) were common triggers of paroxysmal atrial tachyarhythmias, which could be eliminated by cryoablation of extrinsic sympathovagal nerves [2]. Chen and colleagues [3,4] found that infusion of nerve growth factor or applying electrical stimulation to the LSG following myocardial infarction increased nerve density and ventricular arrhythmias. Direct nerve activity recording from the LSG in a canine model of sudden cardiac death showed that most ventricular tachycardia (86.3%) and sudden cardiac death were triggered by increased LSG nerve activity [5]. Interventions that decrease nerve activity of LSG are often antiarrhythmic. For example, inhibition of LSG nerve activity by chronic low-level vagus nerve stimulation significantly reduces the frequencies of paroxysmal atrial fibrillation (14.8/d versus 9.2/d in sham stimulation group) and atrial tachycardia (8.0/d versus 22.0/d in sham stimulation group) in ambulatory dogs [6]. Clinical evidence has shown that left cardiac sympathetic denervation, e.g. LSG resection, is able to prevent recurrence of malignant ventricular arrhythmias in high-risk patients [7]. These observations suggest that LSG plays an important role in the pathogenesis of cardiac arrhythmias.

Renal sympathetic nerve (RSN), which has been identified as an important mediator of systemic sympathetic tone, may also be involved in the pathogenesis of cardiac arrhythmias. Clinical studies suggest that patients with chronic kidney disease, which is always accompanied by RSN activation, are associated with higher prevalence of atrial fibrillation [8] and sudden cardiac death [9] compared to those without chronic kidney disease. In recent years, RSN has become an interesting intervention target for the treatment of many diseases associated with chronic sympathetic activation [10], including cardiac arrhythmias [11–13]. Linz et al. showed that RSN denervation was able to prevent obstructive sleep apnea-associated atrial fibrillation [14] and acute ischemia-induced ventricular arrhythmias [15]. In a canine model of pacing-induced heart failure, Zhao and colleagues found that RSN denervation could suppress the atrial substrate remodeling and the atrial fibrillation vulnerability [16] as well as the ventricular substrate remodeling and the ventricular tachyarrhythmia vulnerability [17]. In a small human study [11, 9 of the 13 patients (69%) treated with circumferential pulmonary vein isolation (PVI) with RSN denervation had no longer atrial fibrillation recurrences at the 12-month post-ablation follow-up versus 4 of the 14 patients (29%) in the PVI-only group, indicating that RSN denervation significantly reduced atrial fibrillation recurrences when combined with PVI in patients with resistant hypertension. In addition, several case reports [12,13] have recently suggested that RSN denervation is an effective and safe therapy for the treatment of ventricular electrical storm. These results indicate that RSN may be a potential therapeutic target for cardiac arrhythmias.

Recent studies showed that there is an association between LSG and RSN. Hou et al. [18] showed that RSN denervation could reduce atrial fibrillation inducibility and reverse atrial electrophysiological changes in a canine model of hyper-sympathetic activity induced by 3-hour LSG stimulation plus rapid atrial pacing. Tsai et al. [19] recorded LSG nerve activity before and after RSN denervation, and they found that the 24-hour average LSG nerve activity decreased from 275 mV-s at baseline to 233 mV-s 4 weeks after RSN denervation, which was associated with a reduction of paroxysmal atrial tachycardia episodes and duration. Recently, our study [20] showed that 3-hour RSN stimulation was able to increase LSG neuronal activity, and facilitate the incidence
of ventricular arrhythmias during acute myocardial ischemia which was attenuated by LSG ablation. Taken together, these observations suggest that there is a potential link between LSG and RSN. Most of the brainstem regions received inputs from the renal afferents also involve in cardiovascular control [21], therefore afferent signals from the RSN are able to affect nerve activity of LSG by modulating central sympathetic outflow (Fig. 1). In conclusion, both LSG and RSN play an important role in cardiac arrhythmias and the potential link between them may be an important mechanism for cardiac arrhythmias.

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