Spinal cord stimulation protects against atrial fibrillation induced by tachypacing

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BACKGROUND Spinal cord stimulation (SCS) has been shown to modulate atrial electrophysiology and confer protection against ischemia and ventricular arrhythmias in animal models.

OBJECTIVE To determine whether SCS reduces the susceptibility to atrial fibrillation (AF) induced by tachypacing (TP).

METHODS In 21 canines, upper thoracic SCS systems and custom cardiac pacing systems were implanted. Right atrial and left atrial effective refractory periods were measured at baseline and after 15 minutes of SCS. Following recovery in a subset of canines, pacemakers were turned on to induce AF by alternately delivering TP and searching for AF. Canines were randomized to no SCS therapy (CTL) or intermittent SCS therapy on the initiation of TP (EARLY) or after 8 weeks of TP (LATE). AF burden (percent AF relative to total sense time) and AF inducibility (percentage of TP periods resulting in AF) were monitored weekly. After 15 weeks, echocardiography and histology were performed.

RESULTS Effective refractory periods increased by 21 ± 14 ms ($P = .001$) in the left atrium and 29 ± 12 ms ($P = .002$) in the right atrium after acute SCS. AF burden was reduced for 11 weeks in EARLY compared with CTL ($P < .05$) animals. AF inducibility remained lower by week 15 in EARLY compared with CTL animals (32% ± 10% vs 91% ± 6%; $P < .05$). AF burden and inducibility were not significantly different between LATE and CTL animals. There were no structural differences among any groups.

CONCLUSIONS SCS prolonged atrial effective refractory periods and reduced AF burden and inducibility in a canine AF model induced by TP. These data suggest that SCS may represent a treatment option for AF.

KEYWORDS Atrial fibrillation; Spinal cord stimulation; Atrial tachypacing animal models

ABBREVIATIONS **AERP** = atrial effective refractory period; **AF** = atrial fibrillation; **AMS** = automatic mode switch; **ANS** = autonomic nervous system; **AV** = atrioventricular; **EARLY** = intermittent SCS therapy on the initiation of TP; **ERP** = effective refractory period; **LA** = left atrial; **LATE** = intermittent SCS therapy after 8 weeks of TP; **LV** = left ventricular; **RA** = right atrial; **SCS** = spinal cord stimulation; **TP** = tachypacing

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Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia and is associated with increased mortality and morbidity.[1–5] Pharmacologic management of AF remains a first line of therapy, and although radiofrequency ablation is effective at restoring sinus rhythm and reducing the symptoms of AF, a large percentage of patients require more than 1 procedure to maintain sinus rhythm, because of recurrent AF or atrial tachycardia.[6,7] Better treatment options are needed for the long-term management of AF.

Spinal cord stimulation (SCS) delivers electrical stimuli to segments of the spinal cord through implanted electrodes and is used to treat a variety of painful conditions including chronic back pain and refractory angina perctoris.[8,9] The mechanism of action of SCS is based on the gate-control theory of pain perception.[10] SCS induces negative feedback by stimulation of the cells of the substantia gelatinosa, inhibiting nociception. In addition to inhibiting pain, SCS modulates afferent and efferent connections between target organs and the autonomic nervous system (ANS).

Numerous studies have established that the ANS modulates cardiac electrophysiology. In particular, autonomic

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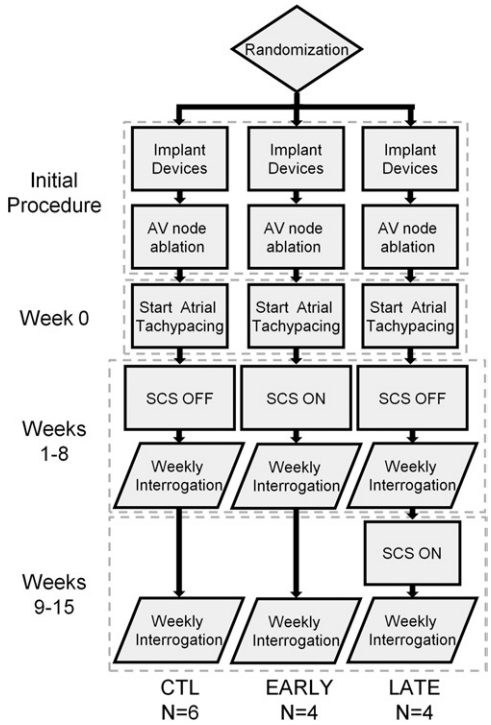

Figure 1 Animal randomization and experimental protocol. AV = atrioventricular; CTL = no SCS therapy; EARLY = intermittent SCS therapy on the initiation of TP; LATE = intermittent SCS therapy after 8 weeks of TP; SCS = spinal cord stimulation; TP = tachypacing.

imbalance contributes to the initiation and maintenance of AF.[11] Vagal stimulation shortens the atrial effective refractory period (ERP) and in some regions of the atria increases dispersion of refractoriness, while stimulation of the stellate ganglion does not alter atrial refractory periods.[12] Excessively unbalanced ANS stimulation causes atrial arrhythmias in animal models, particularly with stimulation of the vagus nerves.[13–17] In humans, paroxysmal AF can be precipitated by autonomic triggers that may be vagal, adrenergic, or mixed.[18] Unlike direct unbalanced stimulation of the ANS, acute modulation of the ANS with SCS reduces the incidence of neuronally induced atrial arrhythmias.[19] However, it is unknown whether SCS is effective at preventing atrial arrhythmias induced by tachypacing (TP) and whether it can suppress arrhythmias in chronic ambulatory animal models of AF. The purpose of this study was to test the hypothesis that SCS reduces AF in a chronic TP animal model.

Methods

An expanded Methods section is available in the online supplemental material available at http://www.hrsonline.org.

Experimental animals

The New York University School of Medicine Institutional Animal Care and Use Committee approved all experiments described.

Protocol

Figure 1 shows a schematic diagram of the experimental protocol. The study period was 15 weeks. Animals were randomized into 3 groups: SCS pulse generators were not to be activated (CTL), SCS pulse generators to be activated at the time of the initiation of atrial TP (EARLY), and SCS pulse generators to be activated 8 weeks after the initiation of atrial TP (LATE). The animals were implanted with cardiac pulse generators, SCS pulse generators, and percutaneous leads. Atrial TP was initiated in all animals 3–21 days after the implant procedure.

Initial procedure

Transthoracic echocardiography was performed after induction of general anesthesia. Epidural SCS leads were positioned in the upper thoracic region (T1–T5; Figure 2) and connected to the SCS pulse generator. Active fixation permanent pacing leads were implanted into the right atrial (RA) appendage and the right ventricle apex and connected to cardiac pulse generators.

An electrophysiology study was conducted in a subset of animals (n = 12) with the SCS pulse generators off (SCS OFF) and then on (SCS ON). Sinus cycle lengths, PR interval, RA ERP, and left atrial (LA) ERP were obtained. For the SCS-ON measurements, SCS pulse generators were activated and measurements were made after 15 minutes of stimulation. Atrioventricular (AV) node ablation was performed following the electrophysiological study.

Echocardiography

Echocardiograms (HDI 5000 SonoCT; Philips Healthcare, Andover, MA) were performed with atrial TP turned off. Left ventricular (LV) wall motion was assessed in multiple views. LA dimension was measured by using the maximum

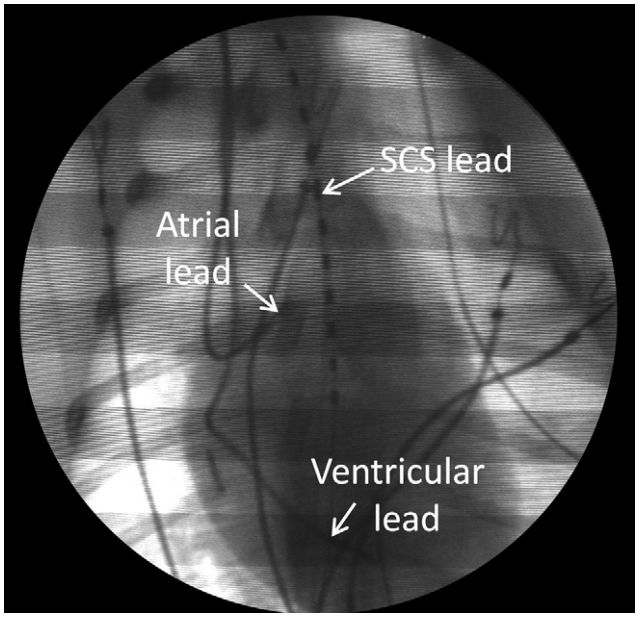

Figure 2 Fluoroscopic image showing the position of the SCS and cardiac pacing leads. SCS = spinal cord stimulation.