Role of Autonomic Nervous System in Cardiac Arrhythmia

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58 YOM With CAD, VF During Treadmill Exercise Testing, Chen et al, JFMA 1979
Nerve Sprouting After Peripheral Nerve Injury

Nerve Growth Factor (NGF)
Growth Associated Protein 43 (GAP43)
S100 stain

Lan S Chen, MD, Childrens Hospital LA and USC Keck School of Med
Nerve Sprouting and Sympathetic Hyperinnervation After MI (Human)
Cao et al, Circulation 2000
Nerve Sprouting and Sympathetic Hyperinnervation After MI (Mouse)
Yong-Seog Oh et al, Heart Rhythm 2006
Background

- MI causes nerve sprouting, sympathetic hyperinnervation and increased sympathetic tone.

- Clinical observations suggest that increased sympathetic tone is important in the initiation of ventricular arrhythmia and SCD.

- However, little direct evidence is available to support a temporal relationship between spontaneous sympathetic discharges and cardiac arrhythmia and SCD in ambulatory animals.
Background

Left Stellate Ganglion (LSG)

Major source of sympathetic innervation to the heart
Hypothesis

Increased left stellate ganglion nerve activity (SGNA) is an immediate trigger of the spontaneous ventricular arrhythmias after myocardial infarction in ambulatory animals.
Sudden Death and Cardiac Sympathetic Nerve Discharge

Left Thoracic Cardiac Nerve Recording

Jardine et al, Clin Auton Res 2003, in an adult Ewe
Sympathetic Nerve Activity and Post-MI Cardiac Arrhythmias

- Methods for continuous 24/7 recording of sympathetic nerve activity in ambulatory, unanesthetized animals
- A high-yield animal model of VT and SCD
First Surgery: Insert DSI Transmitter to a Subcutaneous Pocket and to Record Left SGNA and Subcutaneous ECGs

The signals from the transmitter were recorded by radio receivers in dog cage. The signals were then transmitted to a computer for analyses.
Blood Pressure and SGNA in an open-chest anesthetized dog

SGNA and Heart Rate in an Ambulatory Dog

Jung et al, Heart Rhythm 2005

[Diagram showing A, B, C, and D with time and A.U. scales]
Filtering to reduce noise

Jung et al, Heart Rhythm 2005

A

ECG

Left SGNA before filtering

Left SGNA after filtering

B

30 sec

4 sec
Diurnal Variations of Sympathetic Outflow
Jung et al, Heart Rhythm 2005
Sympathetic Nerve Activity and Post-MI Cardiac Arrhythmias

- Methods for continuous 24/7 recording of sympathetic nerve activity in ambulatory, unanesthetized animals
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**Method of Data Analyses**

- Normal dogs (N=6, Jung et al, Heart Rhythm 2006)
- SCD model (N=8, Zhou et al, MI+AVB+NGF infusion to LSG)
- We manually analyzed the nerve activity preceding the onset of ventricular arrhythmias.
- Computerized analysis to determine integrated nerve activity (INA) over 100 ms time segments one minute before the onset of ventricular arrhythmias.
Two Distinctly Different Patterns of Increased Stellate Ganglion Nerve Activity

HASDA: high amplitude spike discharge activity
LABDA: low amplitude burst discharge activity
In Normal Control Dogs, Both Forms of Increased SGNA can Accelerate Heart Rate

- LABDA: SGNA 0.2 mV, ECG showing 120 bpm and 162 bpm
- HASDA: SGNA 0.6 mV, ECG showing 168 bpm and 192 bpm
In Experimental Group Dogs with Complete AV Block, Elevated SGNA Abruptly Shortens the p-p Intervals as Shown in this Example
HASDA, LABDA and Ventricular Arrhythmogenesis

• Increased stellate ganglion nerve activity may induce ventricular arrhythmias in experimental group but not in the control group.

• HASDA is more often arrhythmogenic than LABDA.
Most HASDA induced either ventricular arrhythmia (21% of 502 episodes) or QRST morphology changes (65% of 502 episodes).
Circadian Pattern of HASDA

Peak at 8-9am
Epileptiform Discharges and HASDA

Lan S Chen and Shengmei Zhou, MD, Unpublished

13 YO boy with partial seizure

Epileptiform Discharges in EEG

Baseline shifts

HASDA in LSG

1 sec
86.3% VT episodes were preceded within 10-15 sec by significantly increased SGNA (N=205)
Integrated SGNA Showed Variable Patterns 60 s Before the Onset of Ventricular Tachycardia

A
Brief high amplitude SGNA

B
Continuous elevation of SGNA 15 s before VT

C
Bursts of LABDA before VT

D
Continuous 20 seconds elevation of SGNA Followed by 3 s pause before VT.

Seconds before the Onset of VT
The Closer to the Onset of VT, the Higher of the Left Stellate Ganglion Nerve Activity

Quantitative analyses of integrated SGNA 60 s before the onset of VT

* P<0.05; ** P<0.01 vs. -60 s; †p<0.05; †† p<0.01 vs. -10 s
SCD was Preceded by Significantly Increased SGNA

A V paced accelerated idioventricular rhythm

11:22:18 AM

ECG

SGNA

B

Onset of VF

11:22:58 AM (cont.)

ECG

SGNA
**Electrical stimulation of LSG paradoxically increased QT and Tpeak-end intervals**

**Before**

- RR = 1421 ms
- QT = 368 ms
- Tpe = 49 ms

**After**

- RR = 1061 ms
- QT = 389 ms
- Tpe = 61 ms

Afterdischarges
Electrical Stimulation of LSG induced VT and VF

VT

Afterdischarges

VF

Afterdischarges
Conclusions

- Two distinct types of LSG nerve activity (HASDA and LABDA) preceded the onset of ventricular arrhythmia and SCD.
- HASDA is much less common, but much more arrhythmogenic.
- Electrical stimulation of LSG increased ventricular transmural heterogeneity of repolarization.
Thank you!