Presenter Disclosure Information
Medtronic, Guidant, St Jude and Cryocath
Donated Research Equipment

Role of Autonomic Nervous System in Cardiac Arrhythmia

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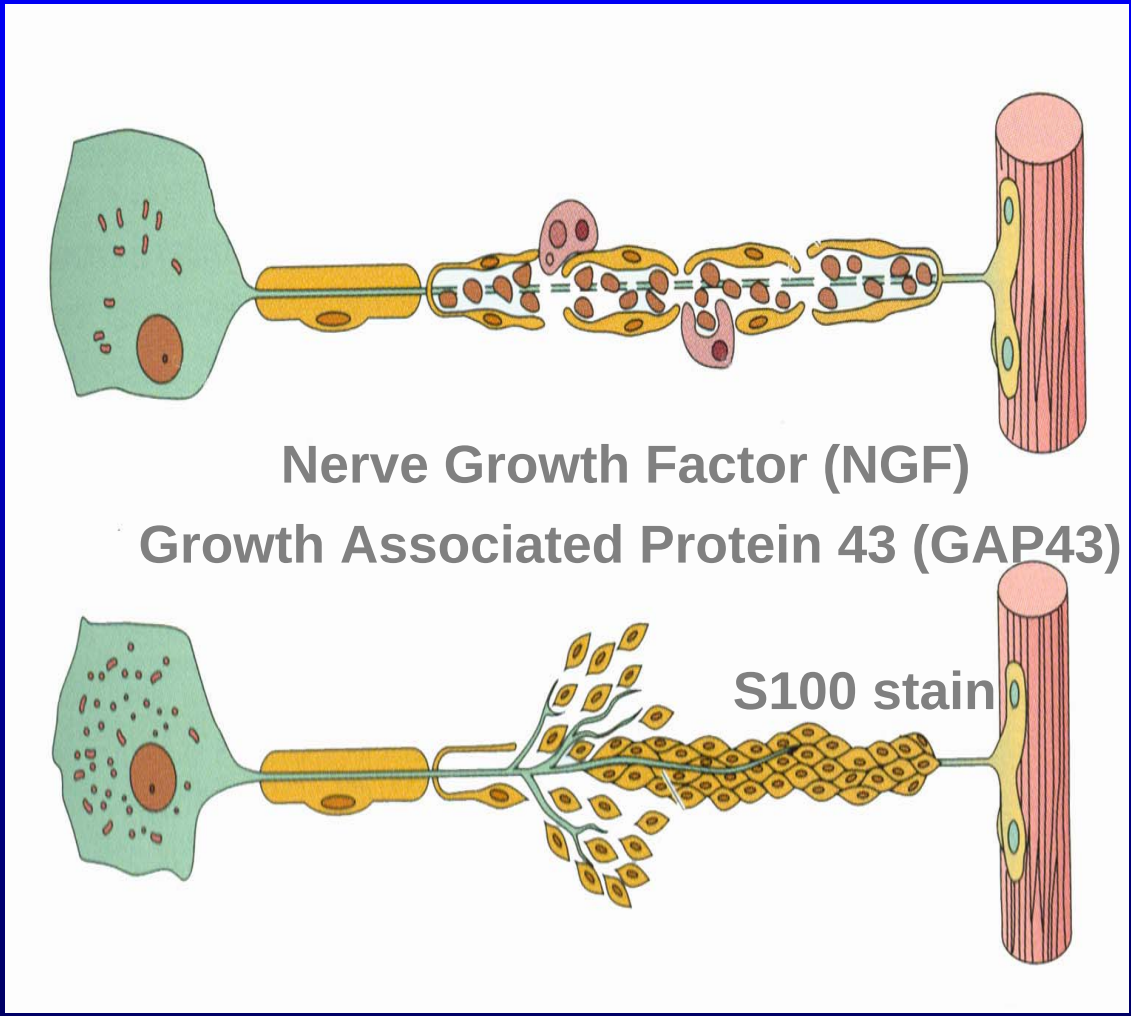
Acknowledgements

Shengmei Zhou, MD
Byung Chun Jung, MD
Yong-Seog Oh, MD
Alex Y. Tan, MD
Vinh Quang Trang, BS
Ghassan Gholmieh, MD, PhD
Michael C. Fishbein, MD
Shien-Fong Lin, PhD
Lan S. Chen, MD

58 YOM With CAD, VF During Treadmill Exercise Testing, Chen et al, JFMA 1979

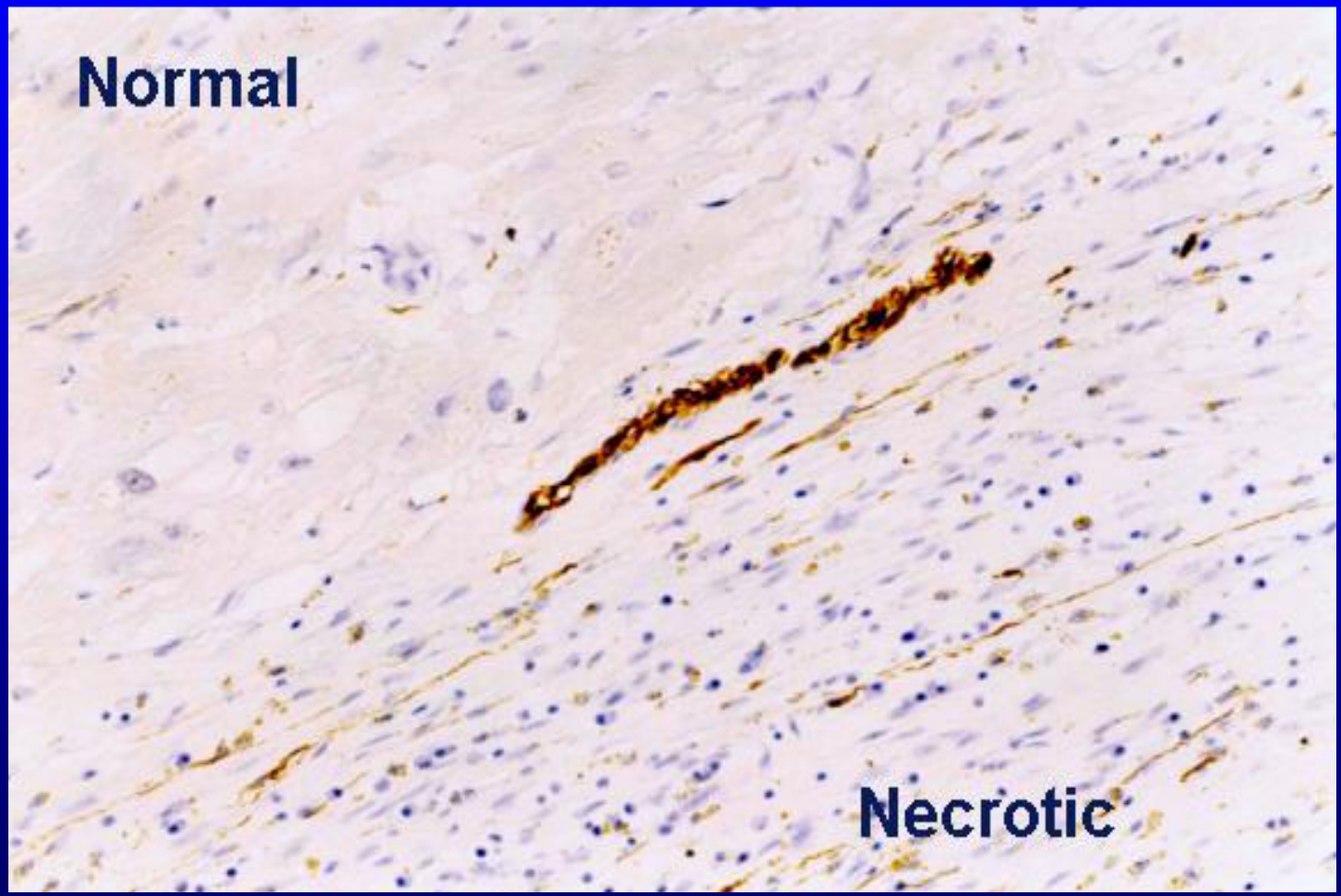
Nerve Sprouting After Peripheral Nerve Injury



Lan S Chen, MD, Childrens Hospital LA and USC Keck School of Med

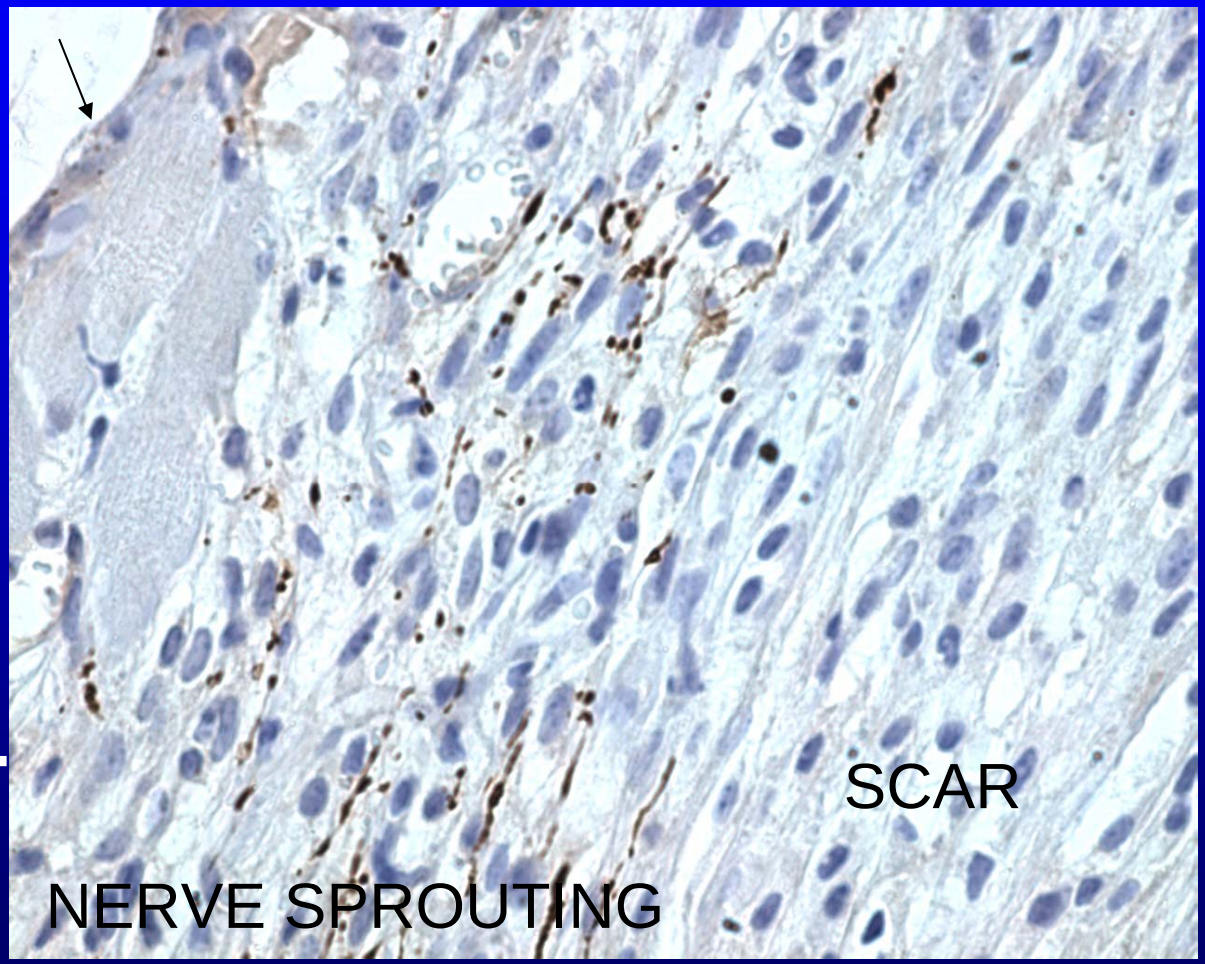
Nerve Sprouting and Sympathetic Hyperinnervation After MI (Human)

Cao et al, Circulation 2000



Nerve Sprouting and Sympathetic Hyperinnervation After MI (Mouse)

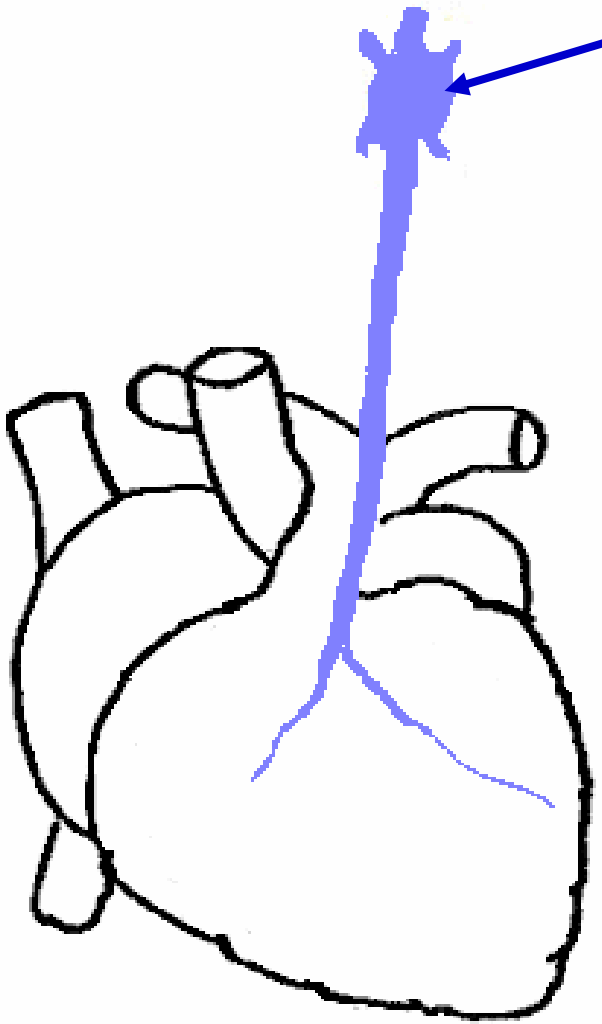
Yong-Seog Oh et al, Heart Rhythm 2006



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

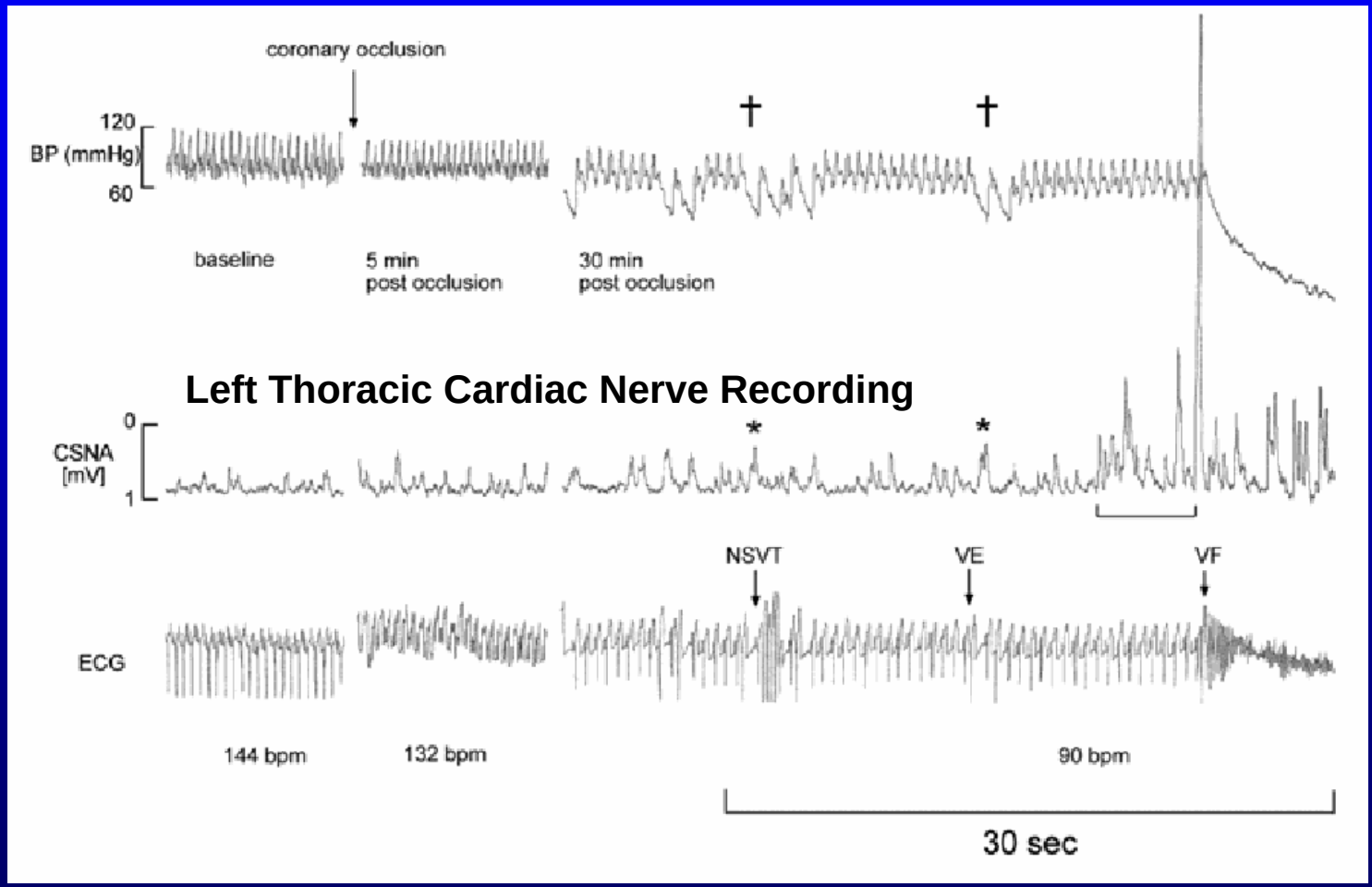
(LSG)

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



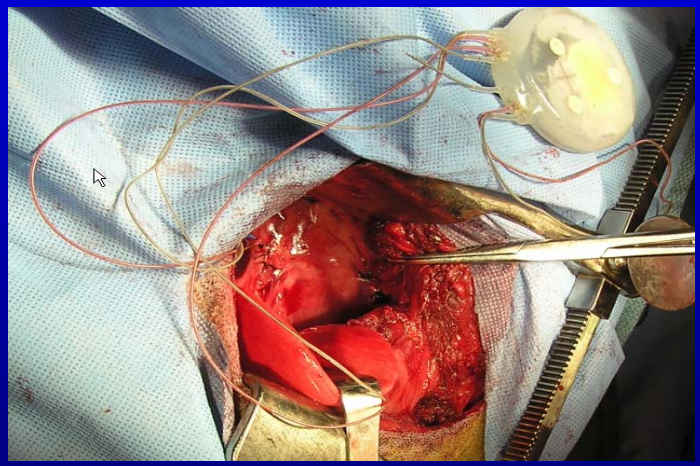
Jardine et al, Clin Auton Res 2003, in an adult Ewe

Sympathetic Nerve Activity and Post-MI Cardiac Arrhythmias

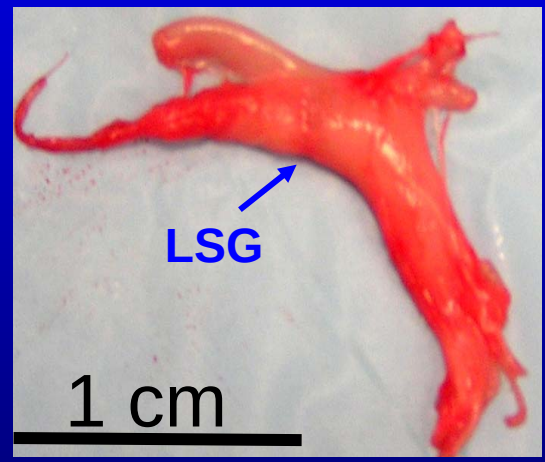
- Methods for continuous 24/7 recording of sympathetic nerve activity in ambulatory, unanesthetized animals
- A high-yield animal model of VT and SCD

First Surgery: Insert DSI Transmitter to a Subcutaneous Pocket and to Record Left SGNA and Subcutaneous ECGs

DSI transmitter

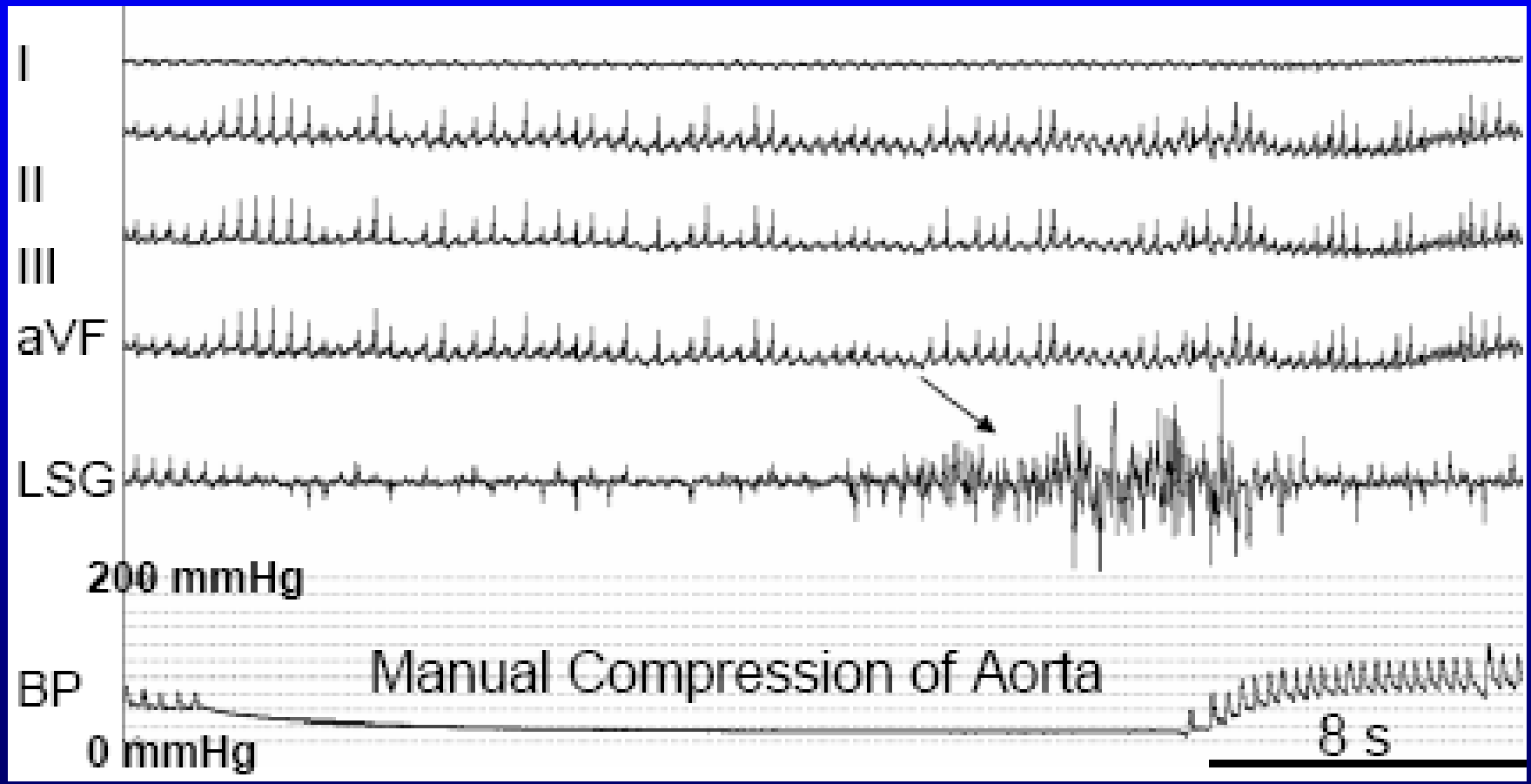


Transmitter



The signals from the transmitter were recorded by radio receivers in dog cage. The signals were then transmitted to a computer for analyses.

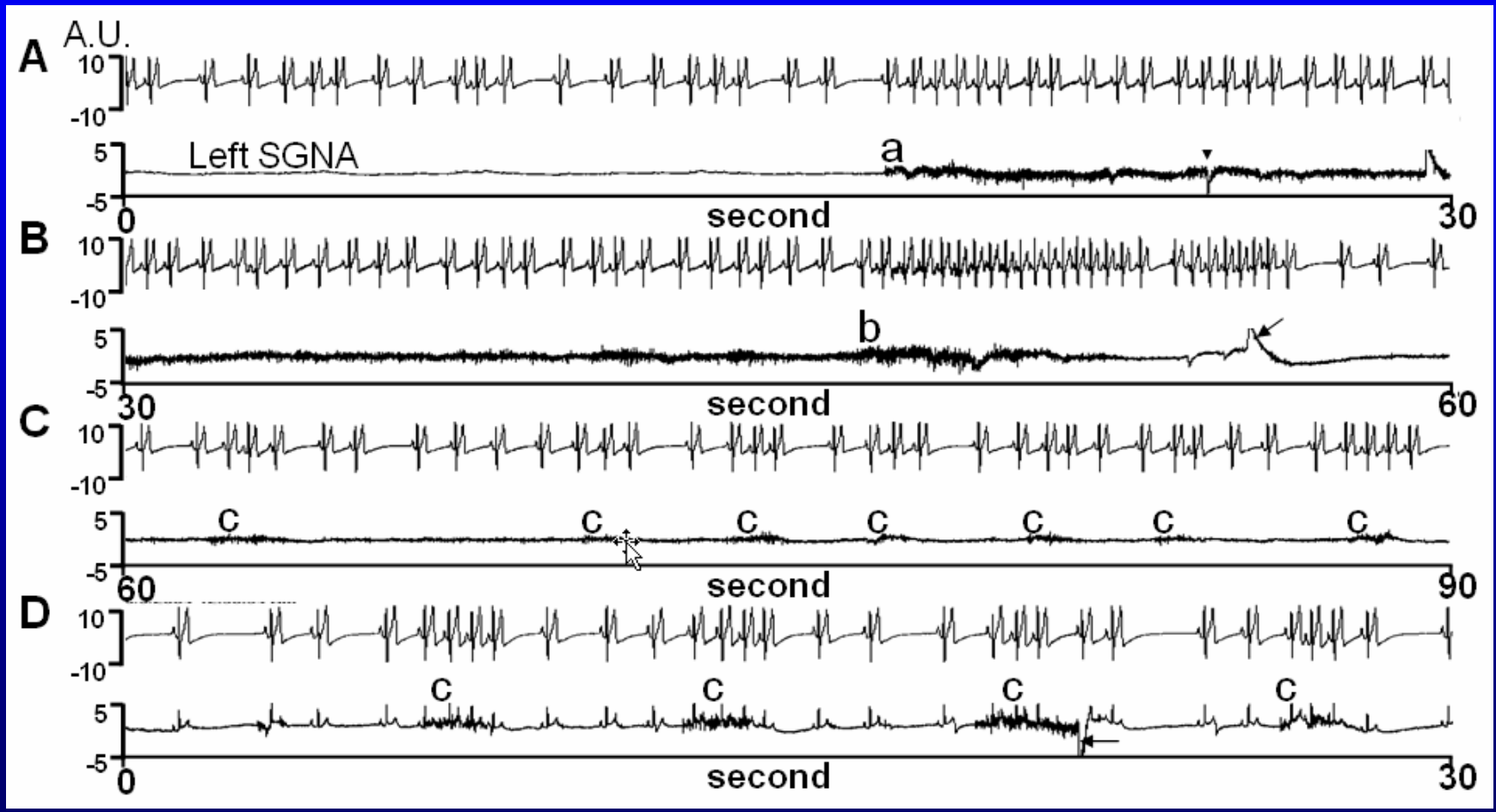
Blood Pressure and SGNA in an open-chest anesthetized dog



Zhou S, Tan A, Ogawa M et al (unpublished)

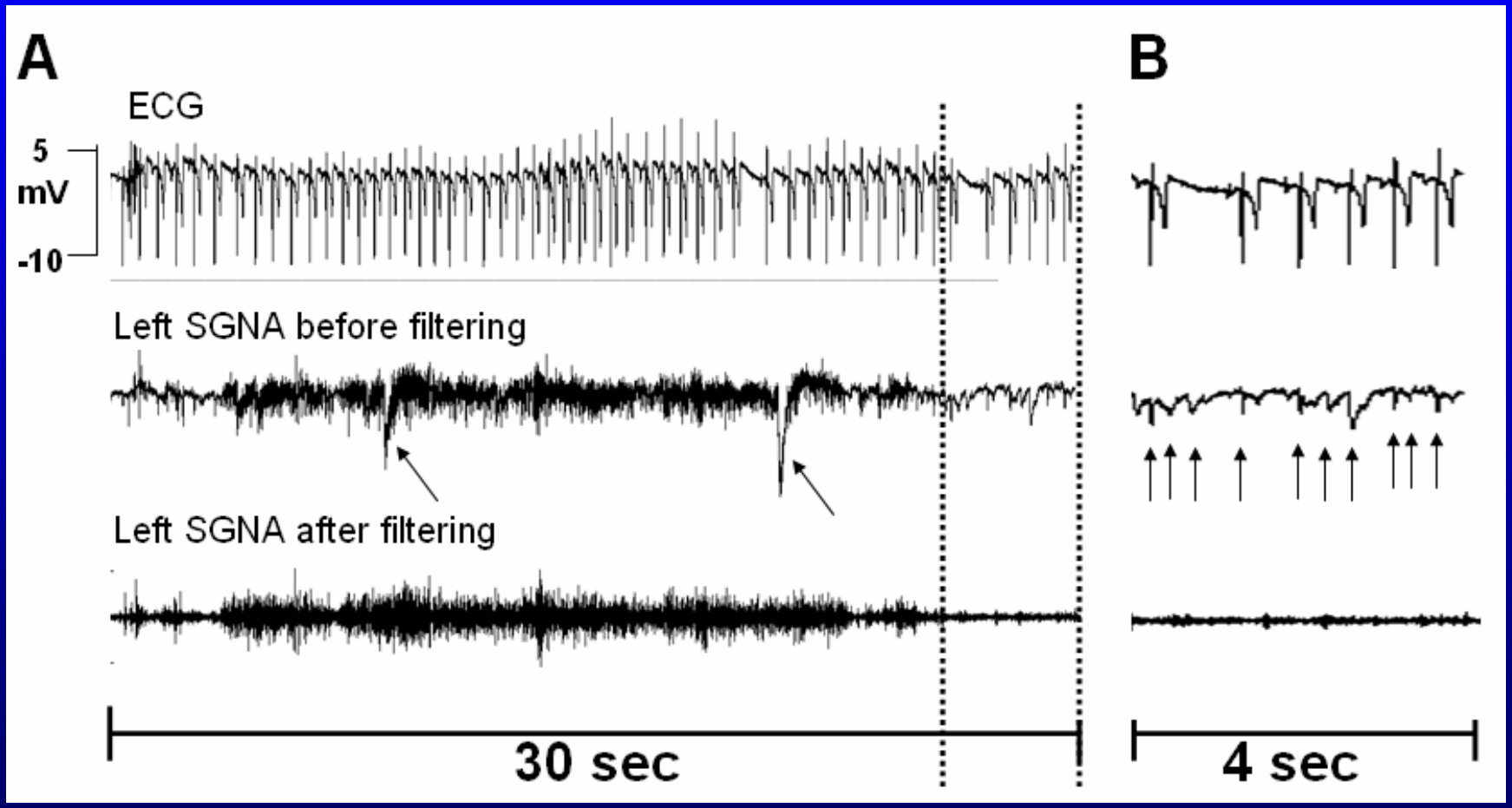
SGNA and Heart Rate in an Ambulatory Dog

Jung et al, Heart Rhythm 2005



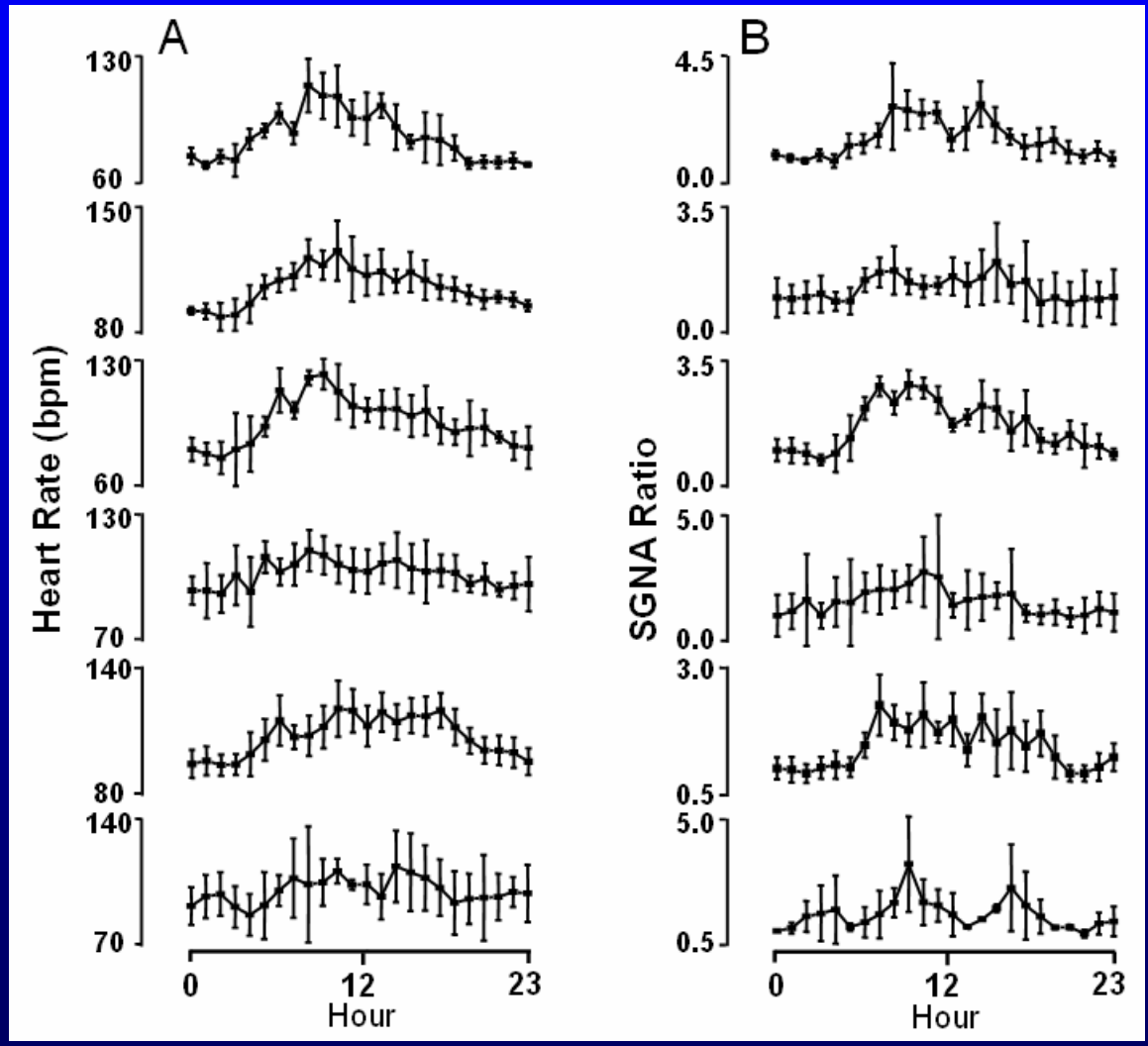
Filtering to reduce noise

Jung et al, Heart Rhythm 2005



Diurnal Variations of Sympathetic Outflow

Jung et al, Heart Rhythm 2005



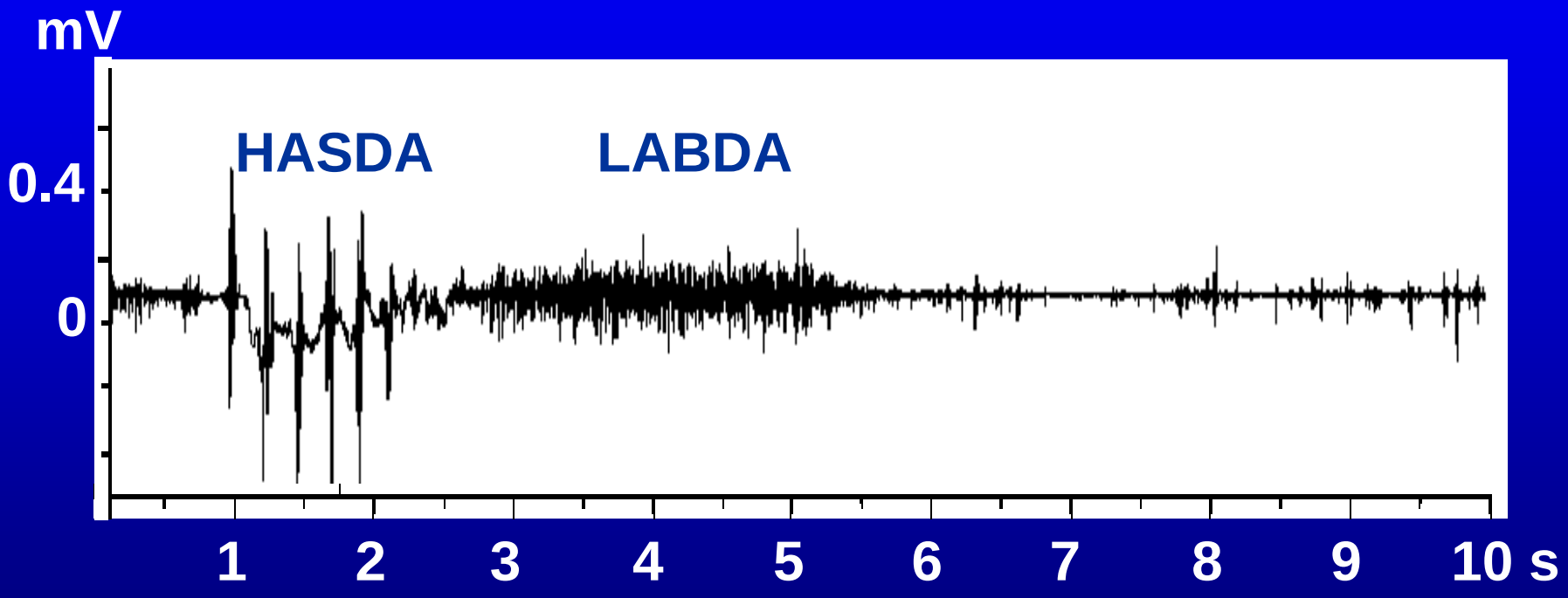
Sympathetic Nerve Activity and Post-MI Cardiac Arrhythmias

- Methods for continuous 24/7 recording of sympathetic nerve activity in ambulatory, unanesthetized animals
- A high-yield animal model of VT and SCD

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.

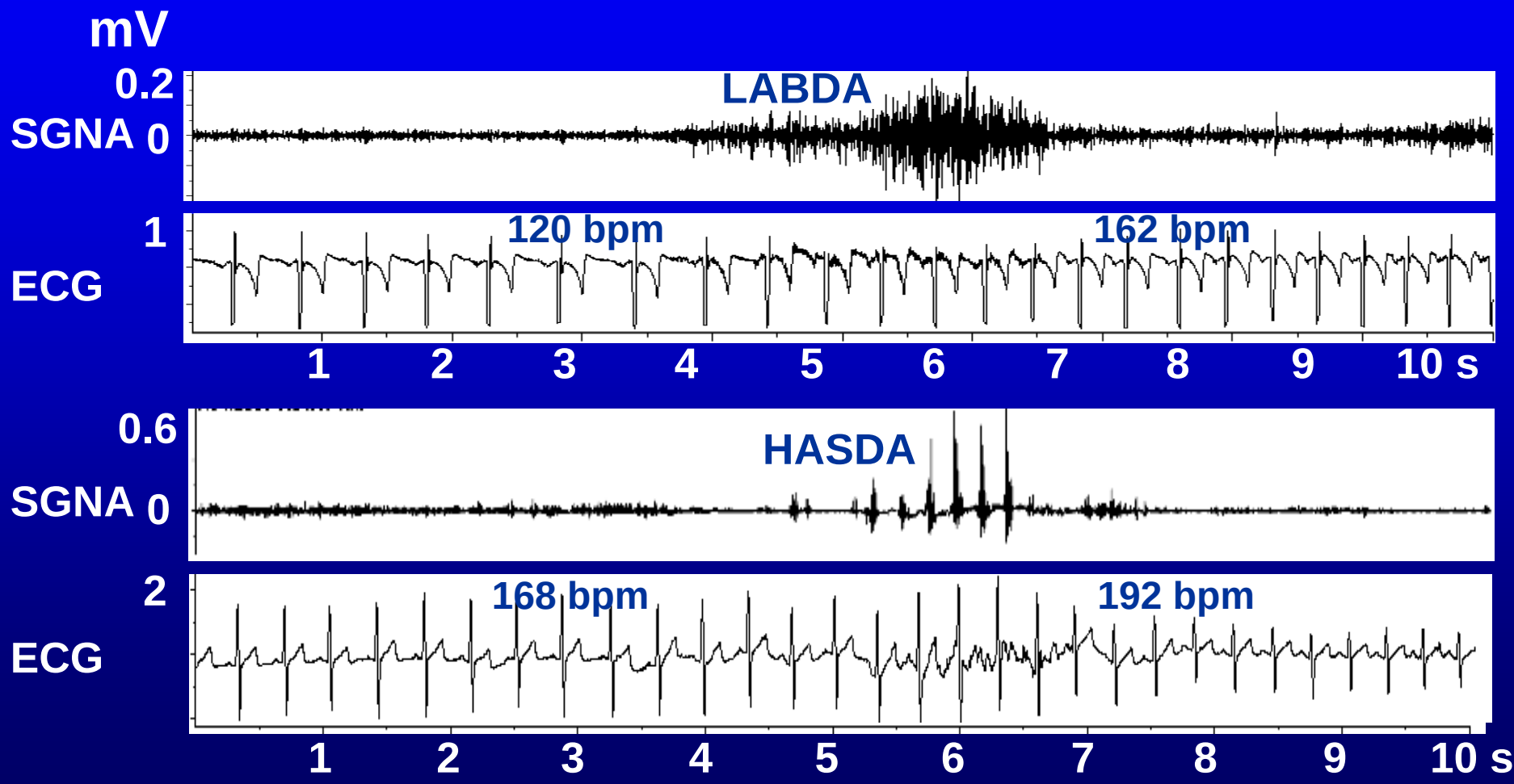
Two Distinctly Different Patterns of Increased Stellate Ganglion Nerve Activity



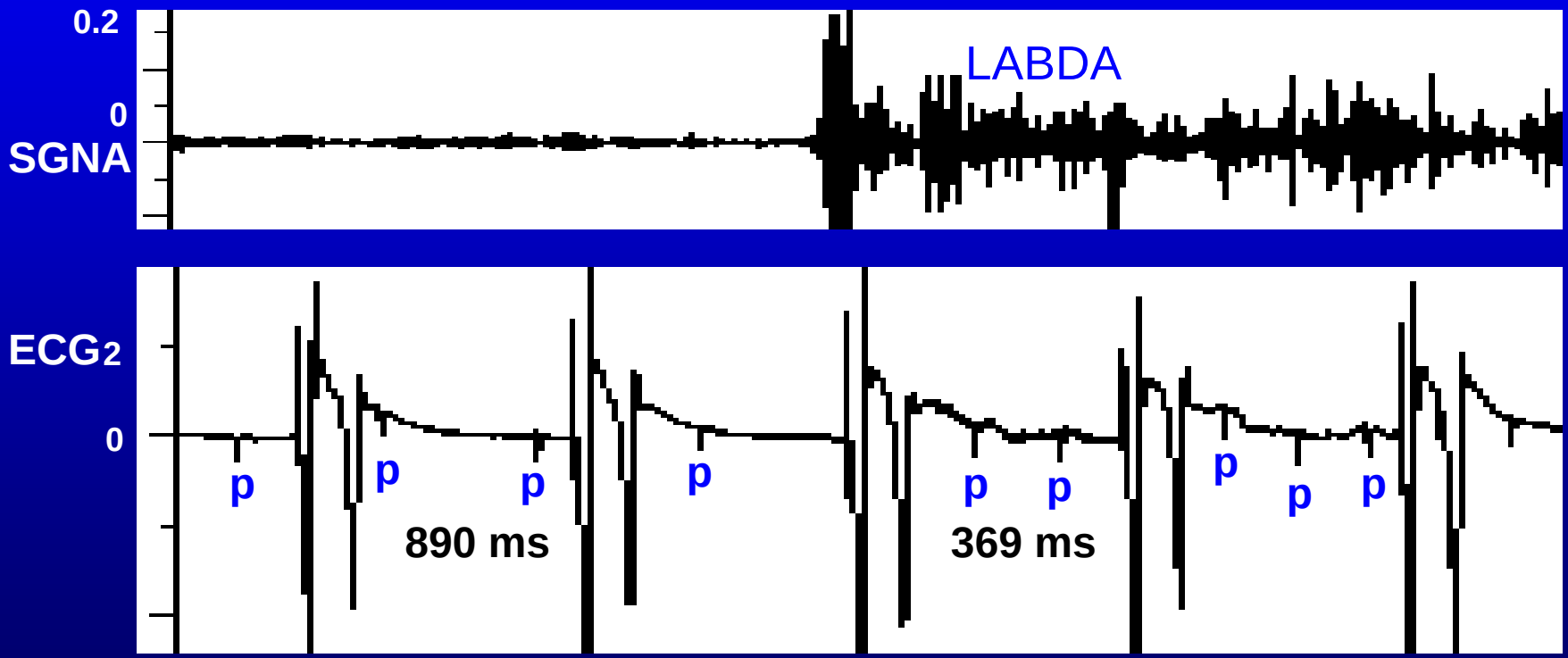
HASDA: high amplitude spike discharge activity

LABDA: low amplitude burst discharge activity

In Normal Control Dogs, Both Forms of Increased SGNA can Accelerate Heart Rate



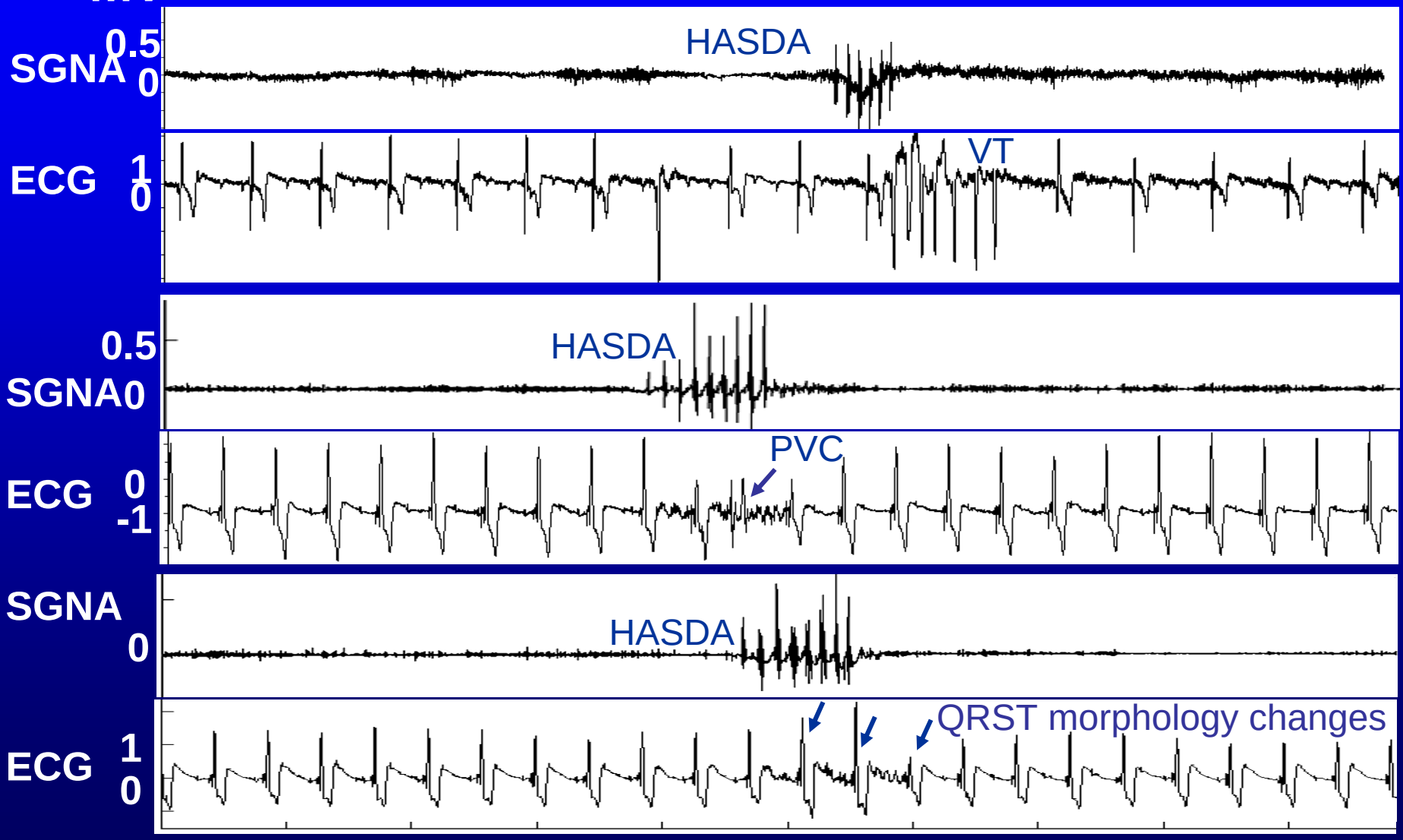
In Experimental Group Dogs with Complete AV Block, Elevated SGNA Abruptly Shortens the p-p Intervals as Shown in this Example



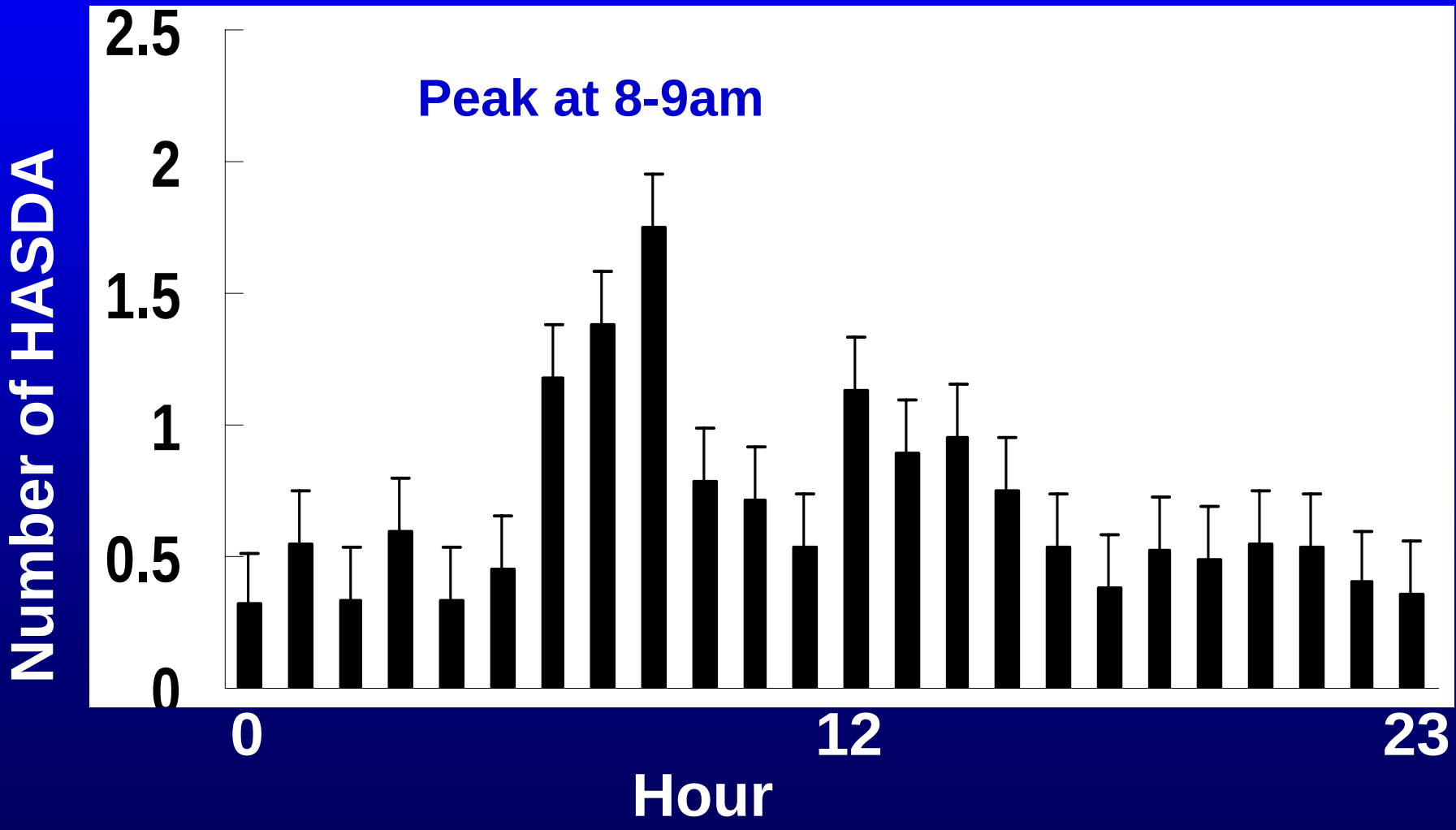
HASDA, LABDA and Ventricular Arrhythmogenesis

- 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)



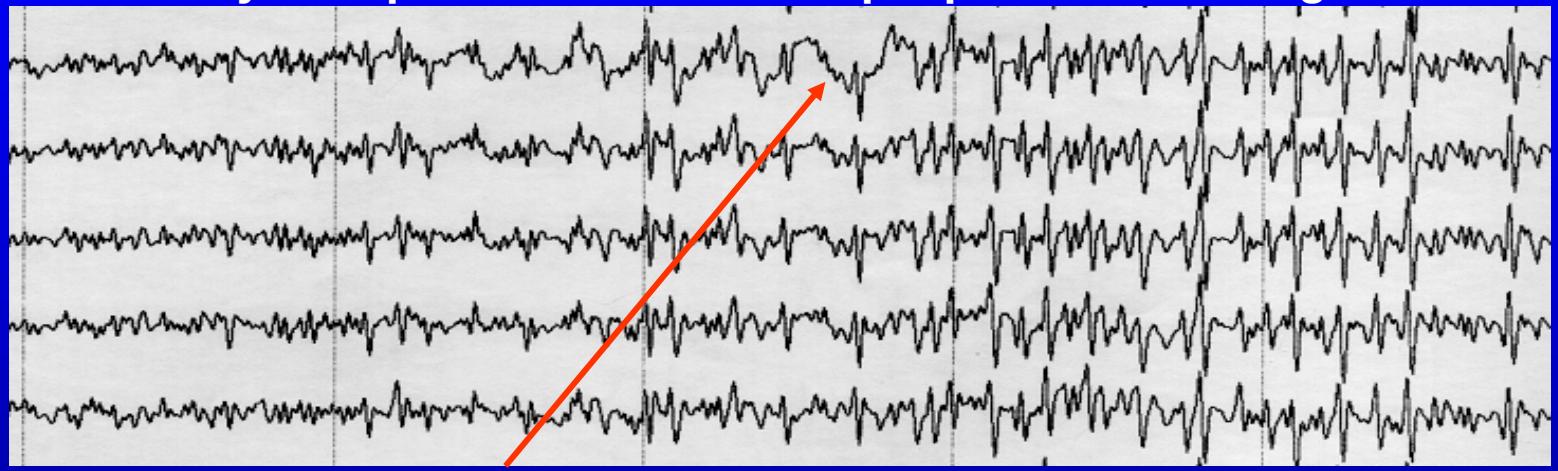
Circadian Pattern of HASDA



Epileptiform Discharges and HASDA

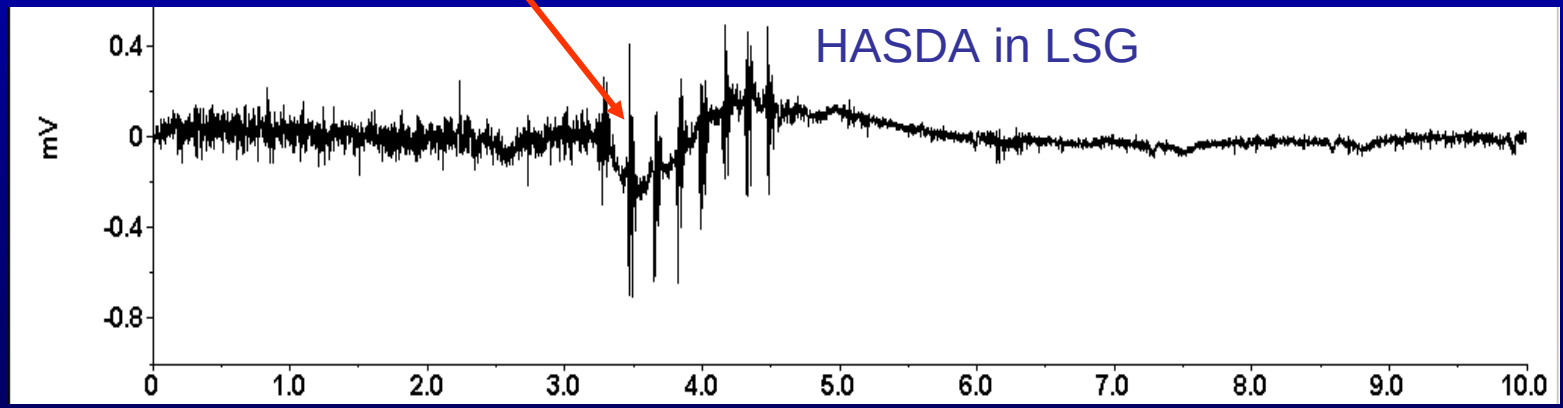
Lan S Chen and Shengmei Zhou, MD, Unpublished

13 YO boy with partial seizure **Epileptiform Discharges in EEG**

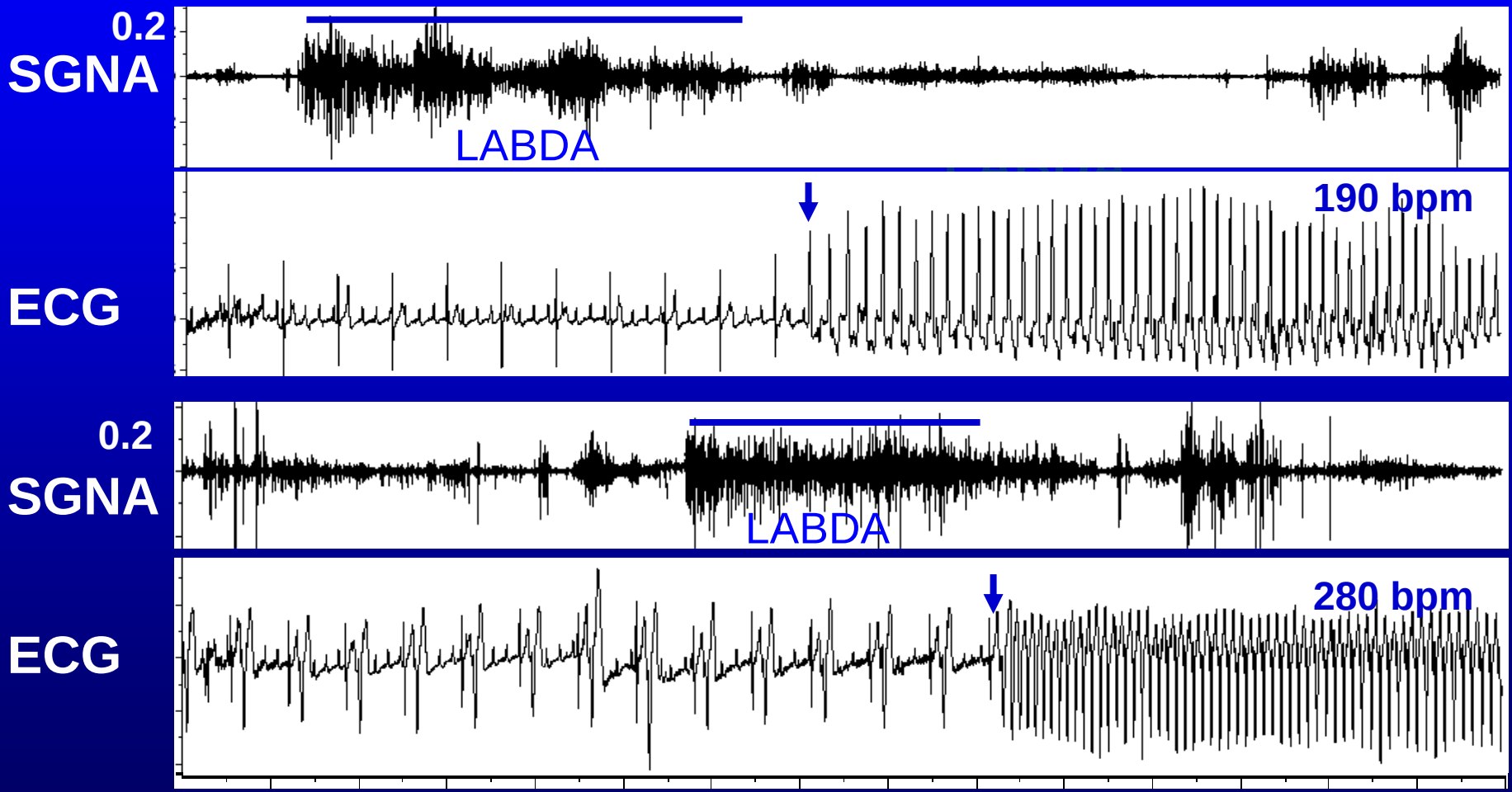


Baseline shifts

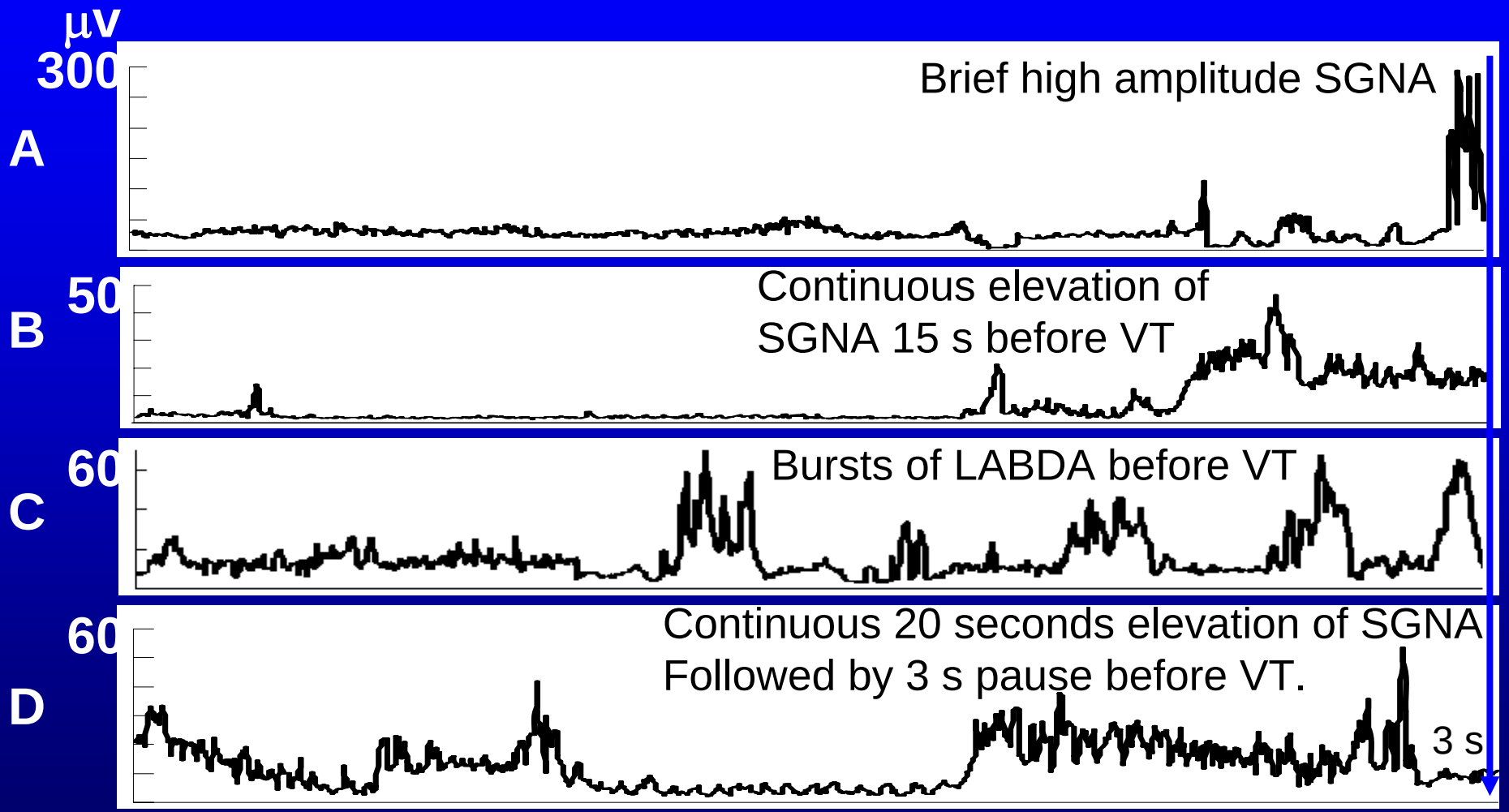
1 sec



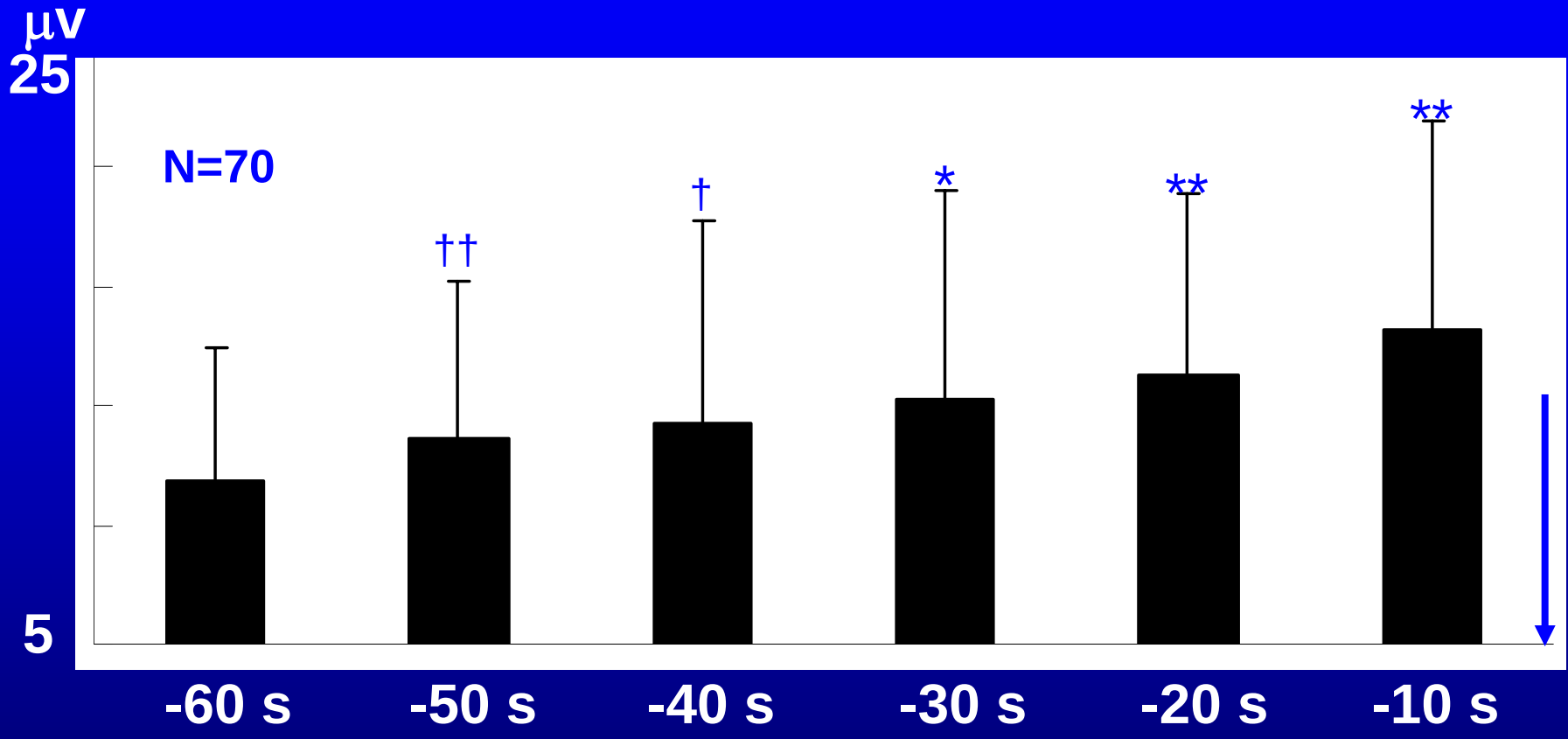
86.3% VT episodes were preceded within 10-15 sec by significantly increased SGNA (N=205)



Integrated SGNA Showed Variable Patterns 60 s Before the Onset of Ventricular Tachycardia



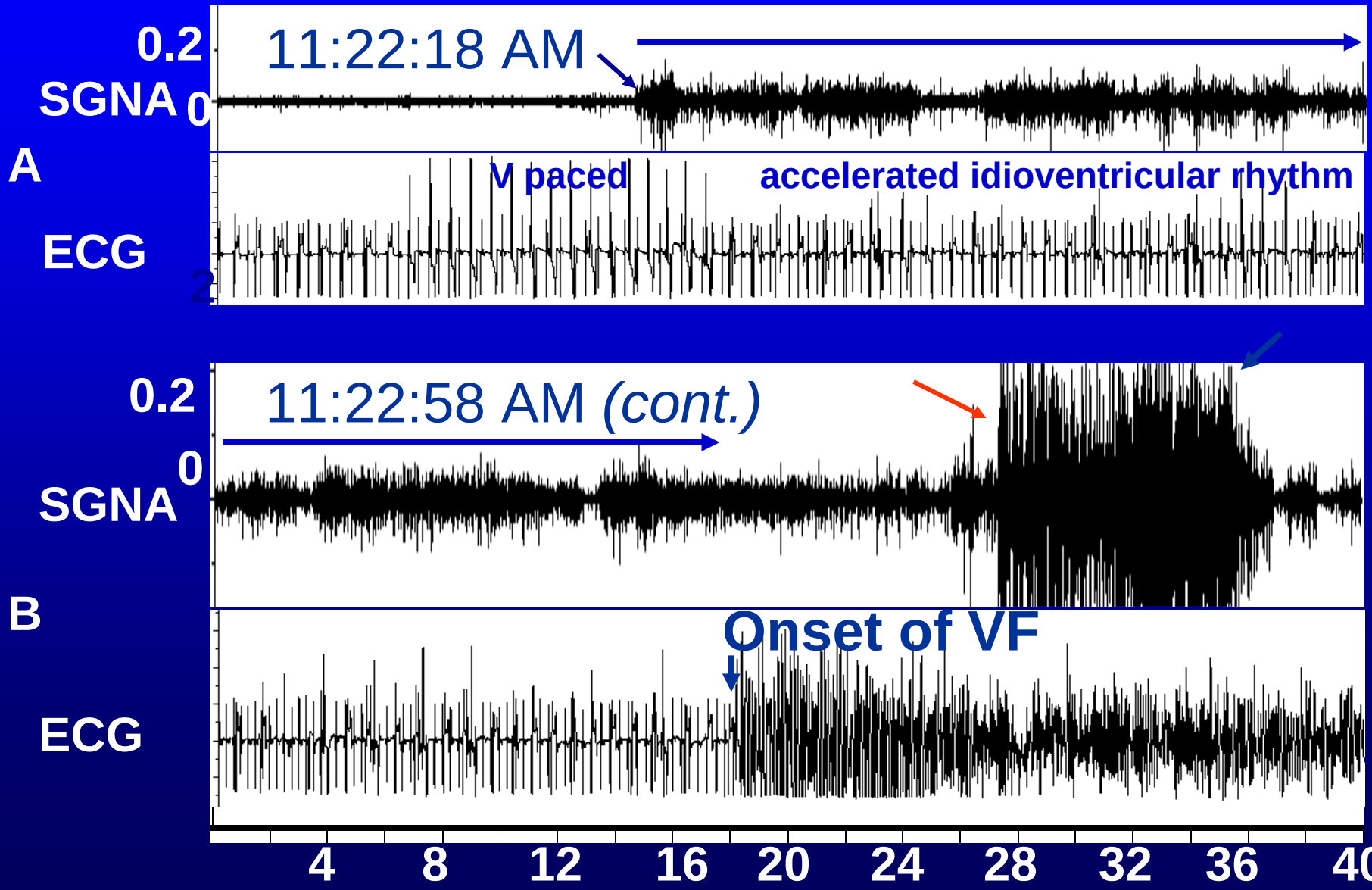
The Closer to the Onset of VT, the Higher of the Left Stellate Ganglion Nerve Activity



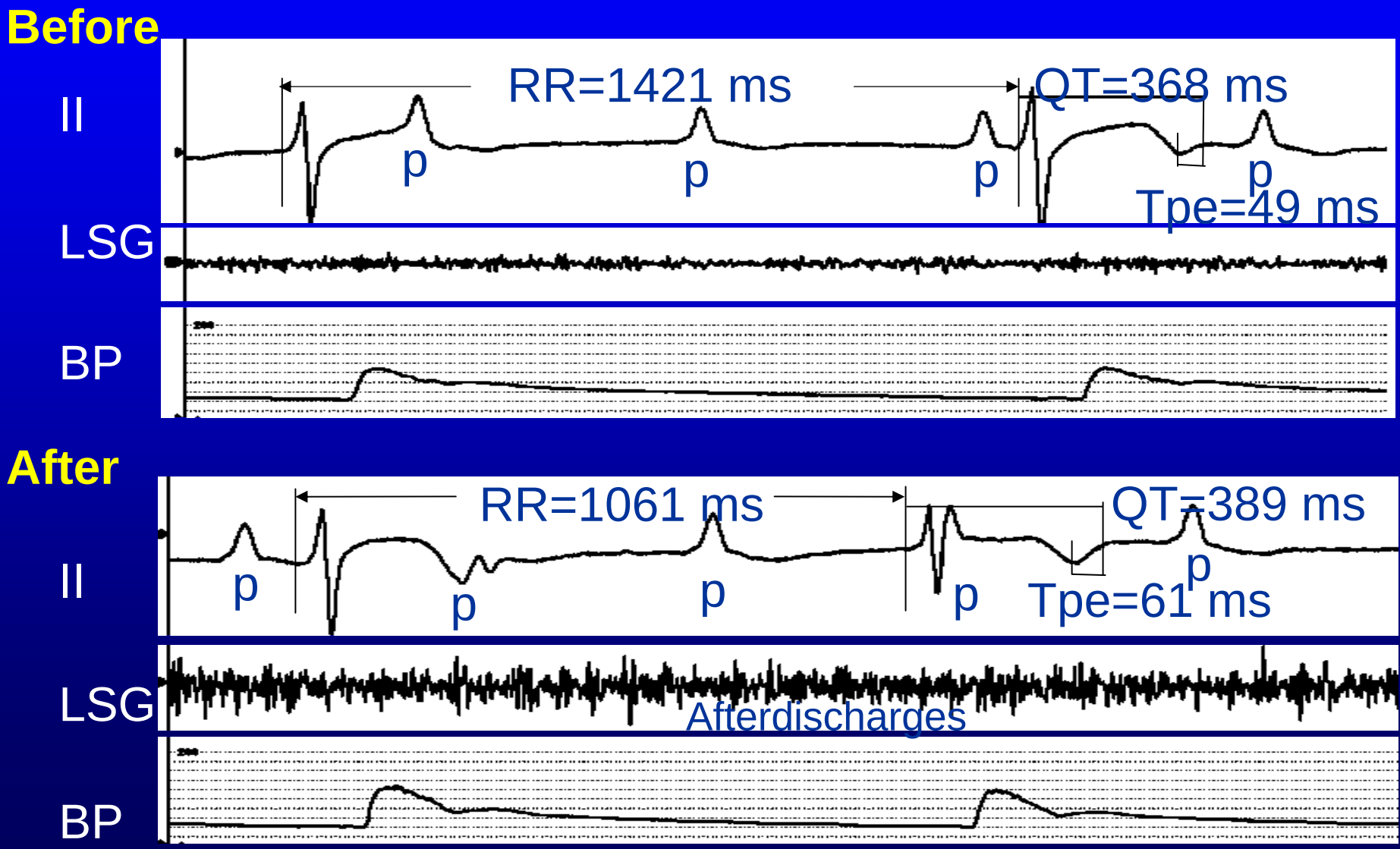
* P<0.05; ** P<0.01 vs. -60 s; †p<0.05; †† p<0.01 vs. -10 s

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

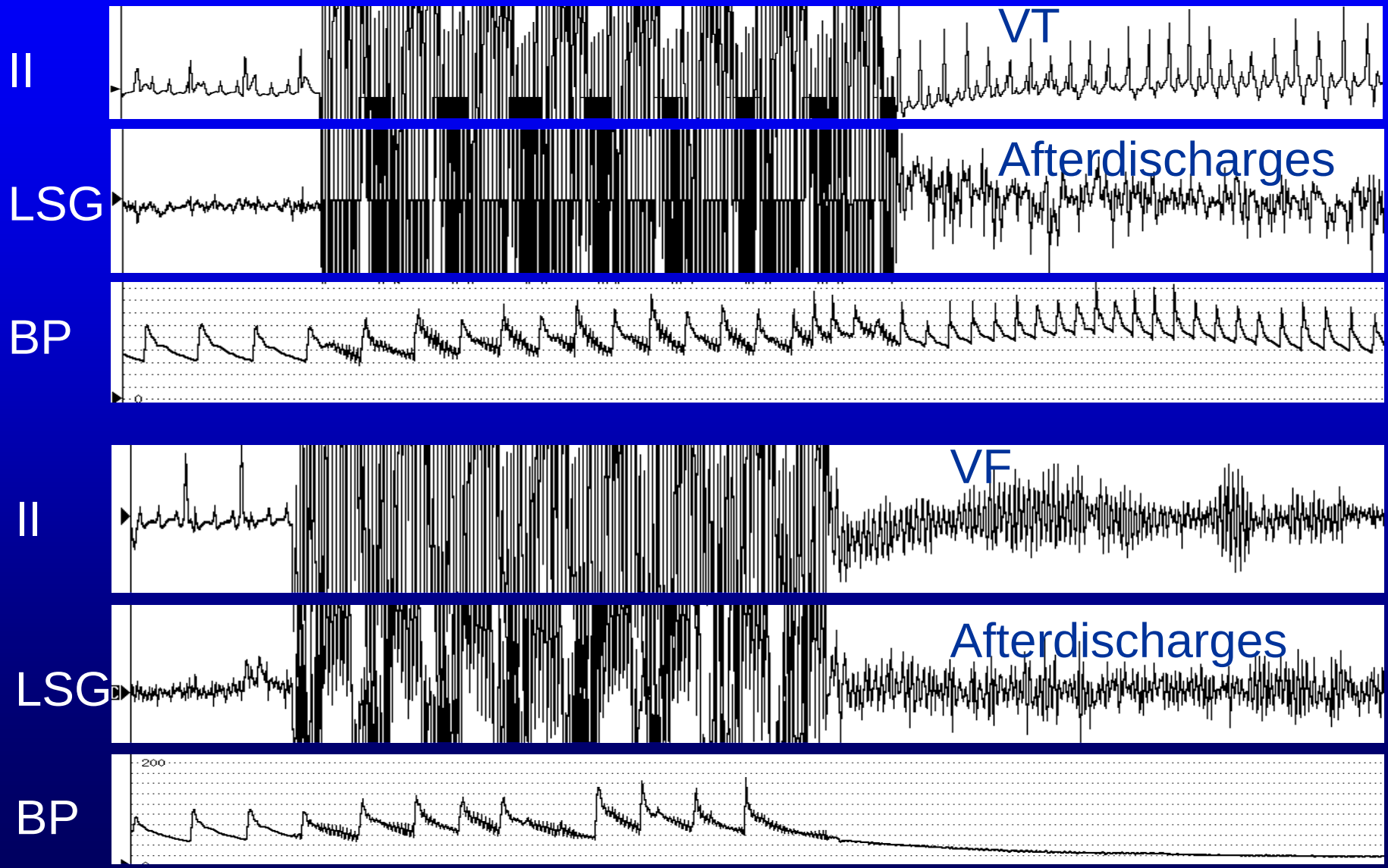
SCD was Preceded by Significantly Increased SGNA



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



Electrical Stimulation of LSG induced VT and VF



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!