



Bidirectional Brain-Body Interactions in Health & Disease: The Heart as a Use Case

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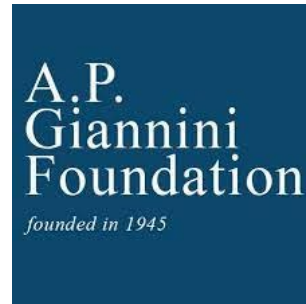
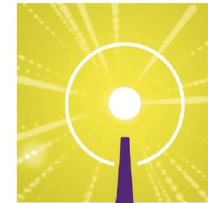
Disclosures

Medtronic, Biotronik, Abbott, Merck, Synchron & Biosense
Webster (Consulting/Honoraria, Research grants)

NeuCures Inc, NeuFera Inc
(Co-founder, Equity)

nFference/Anumana (Stock)

The University of California (UCLA) has
patents developed in the areas of cardiac
catheter technology, embolism prevention
technology, minimally invasive methods
for cardiac interventions, cardiac neural
diagnostics and therapeutics



Funding Sources:

NIH/NHLBI

-1P01HL164311

-1R01HL167885

-1R01HL159001

-1R01HL162717

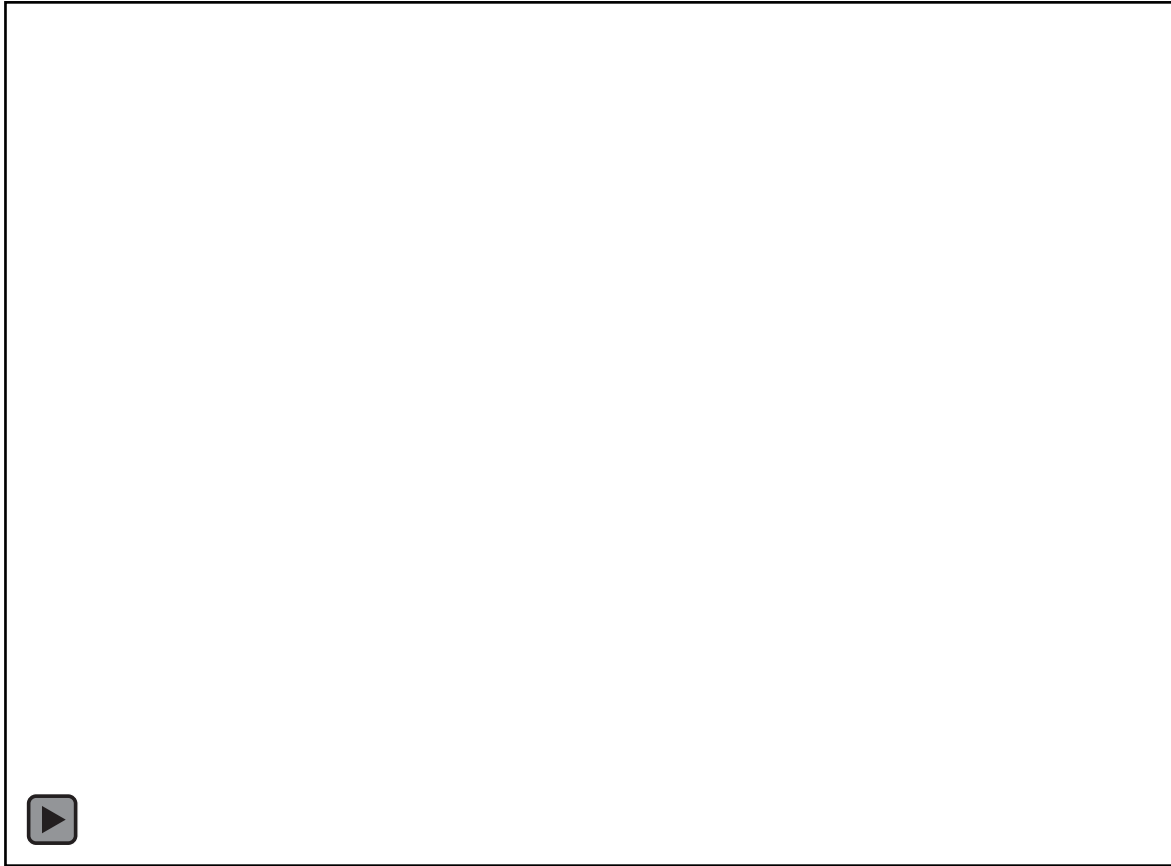
NIH/NIGMS

-T32GM008042

Leducq Foundation
American Heart Association
Chan Zuckerberg Initiative
Heart Rhythm Society
A.P. Giannini Foundation

UCLA CTSI
UCLA STAR Program

A neurocardiologist's perspective



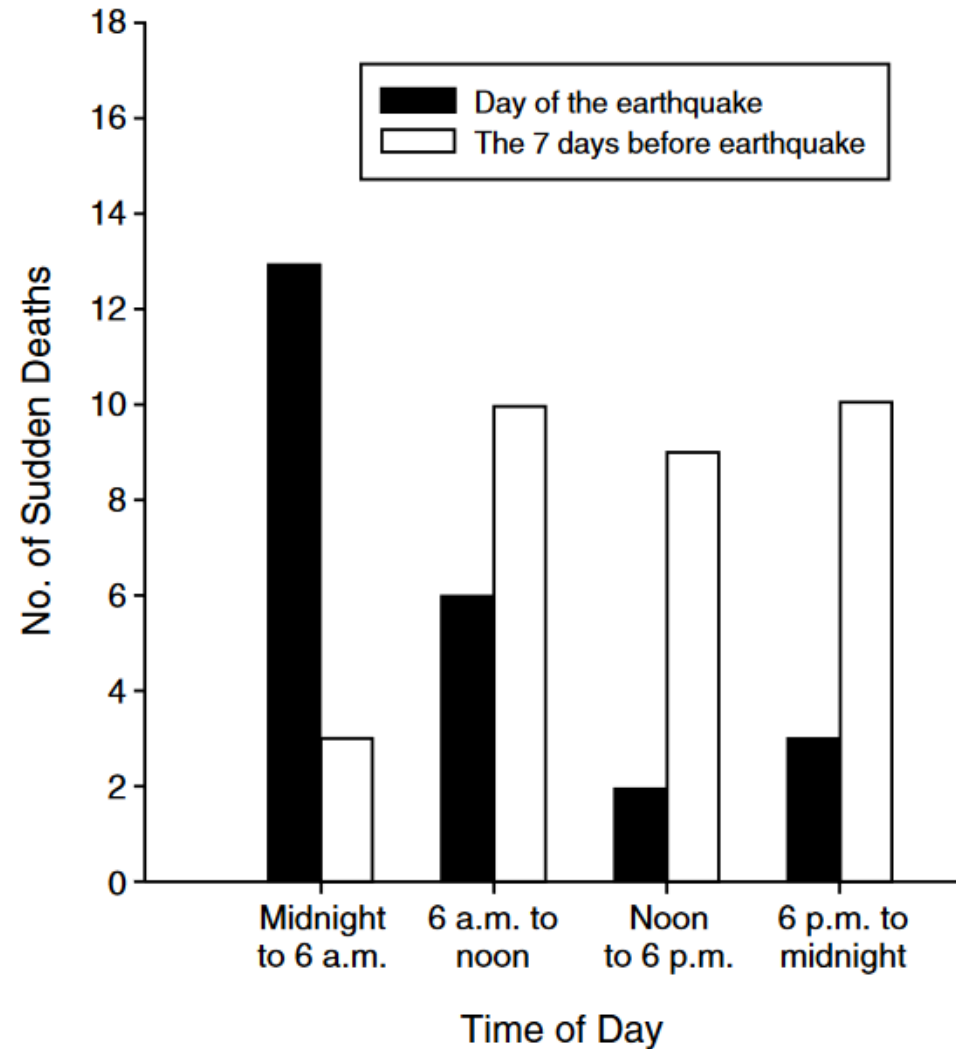
Digest

Rajendran et al. 2016

- Organized as multiple feedback loops
- Ensures that the heart is working on a beat by beat basis
- Responds in short and long time scales to perturbations in cardiac function



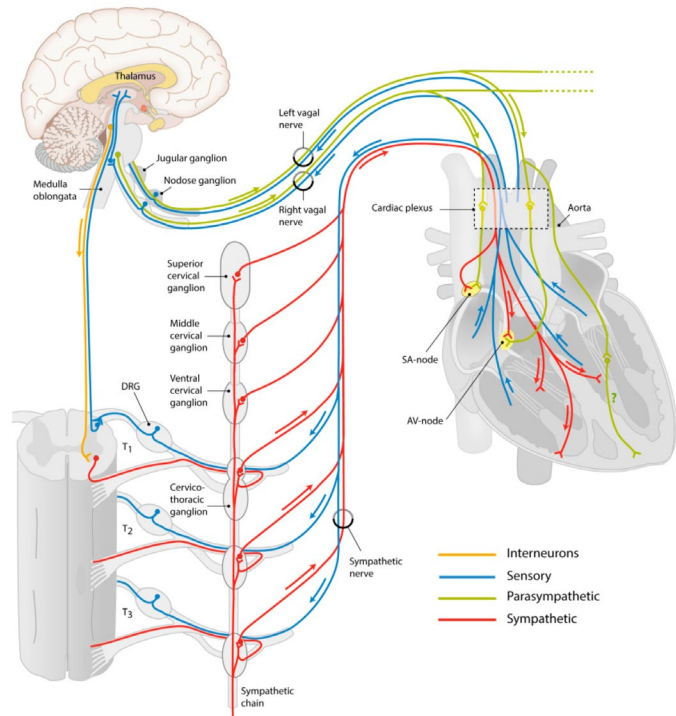
Sudden cardiac death triggered by an earthquake



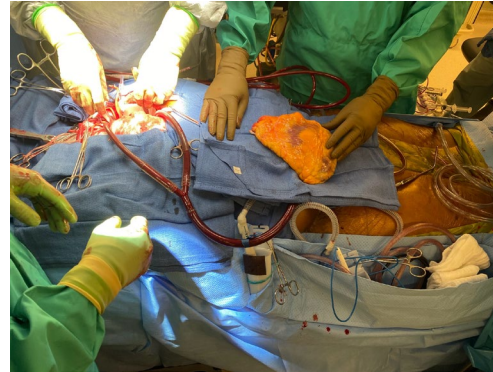
Top-down cardiac neural control & sudden cardiac death



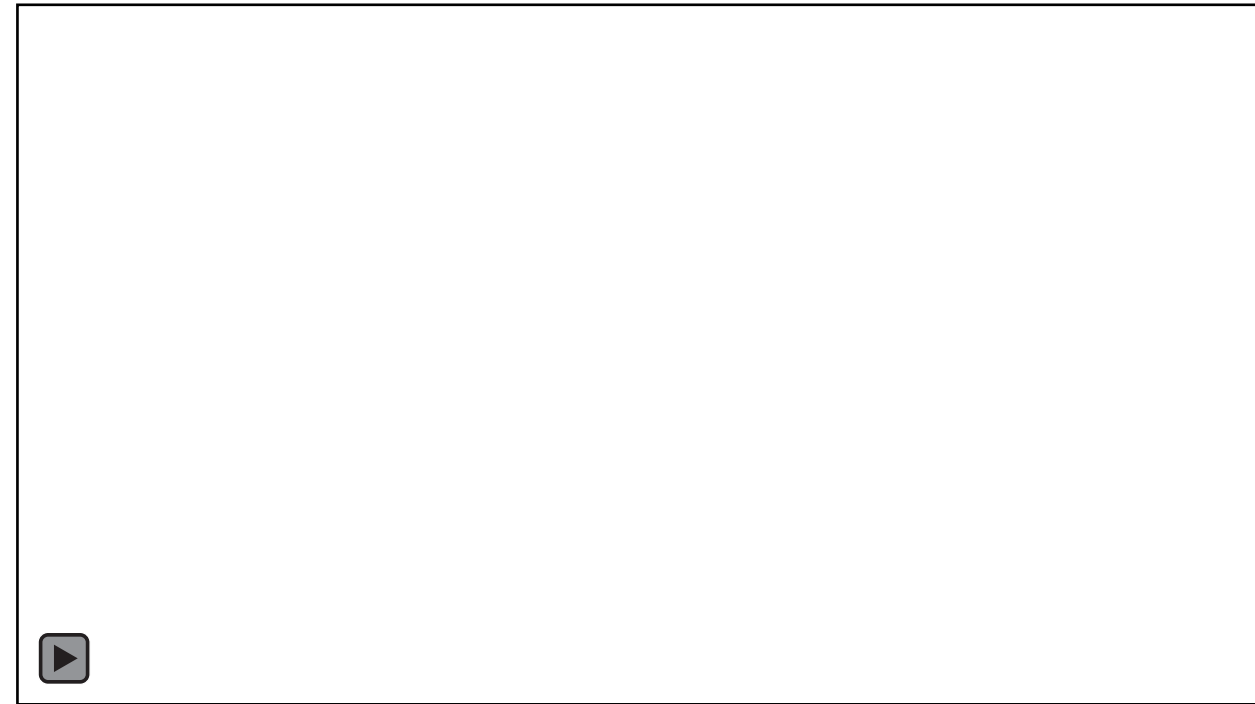
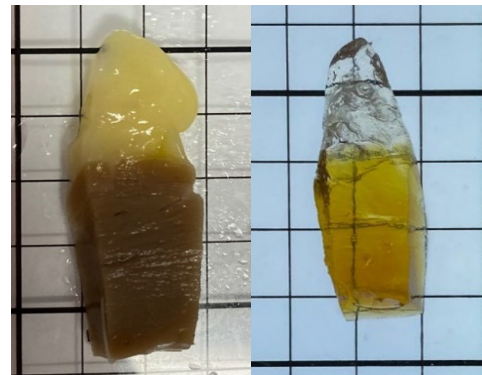
Peter Hanna MD PhD



Human Heart

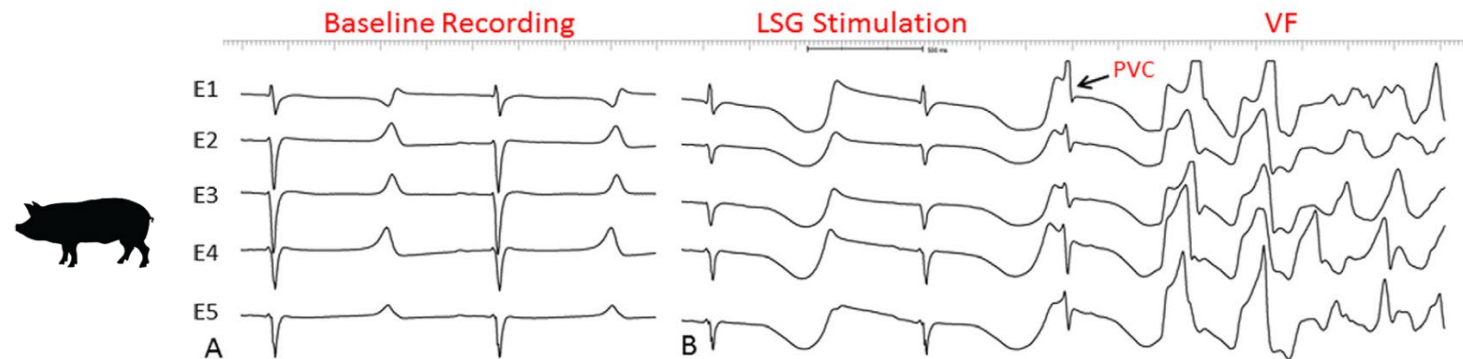
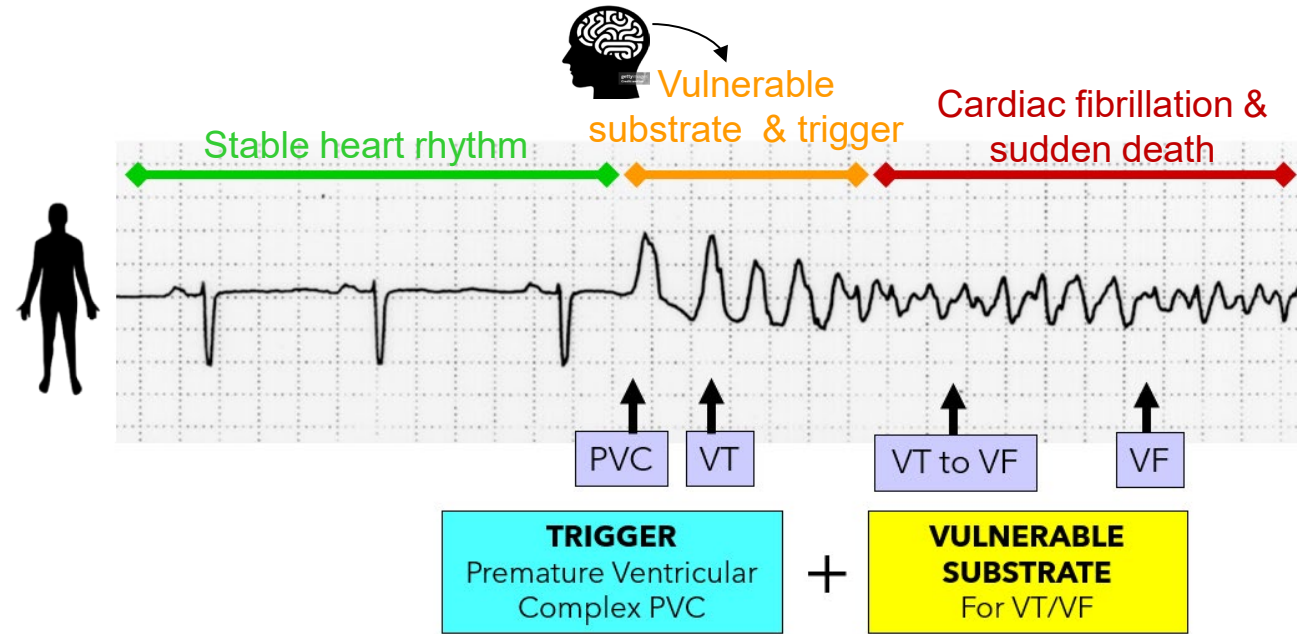
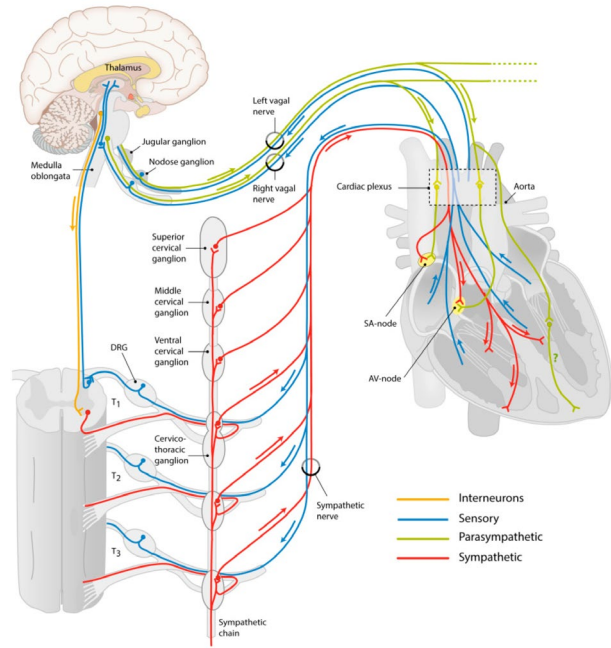


Tissue Clearing



Vegh et al. 2016

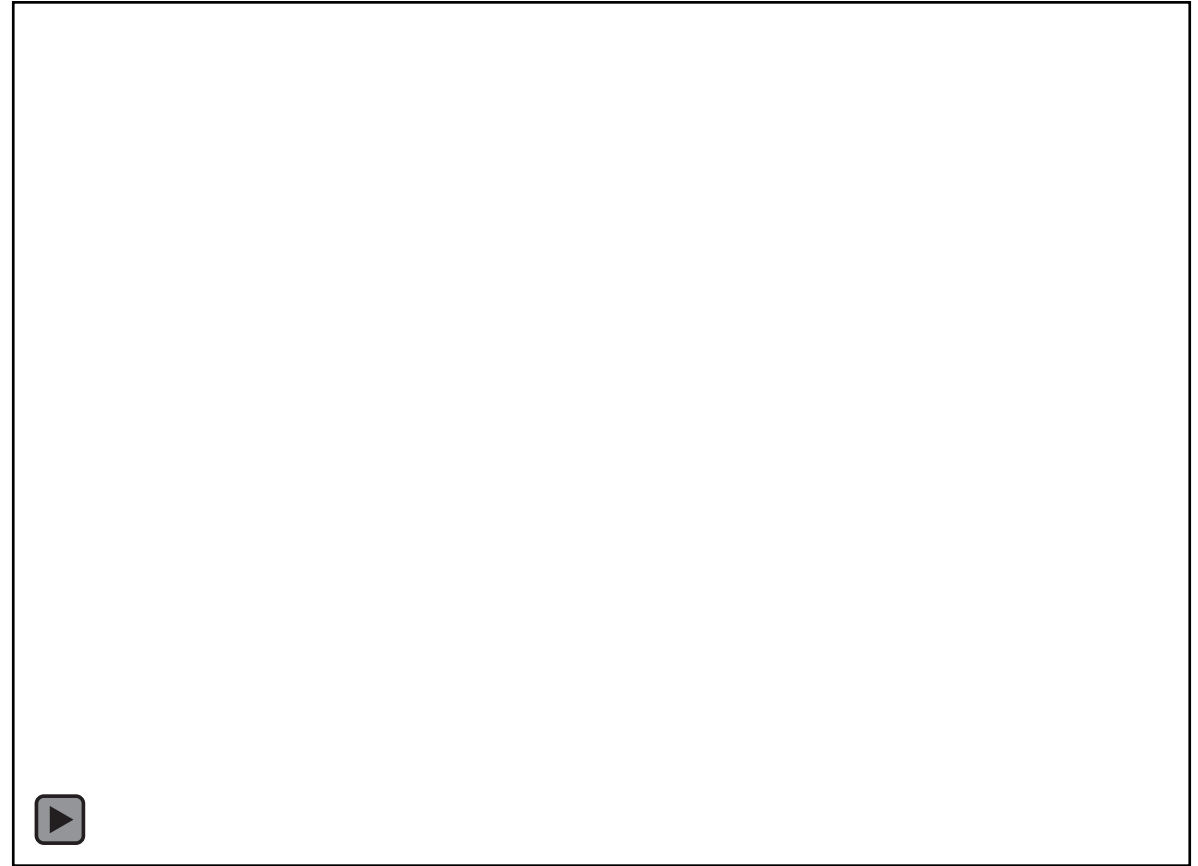
Top-down neural control & sudden cardiac death



Vegh et al. 2016

Heart Rhythm 2012 Aug;9(8):1303-9.

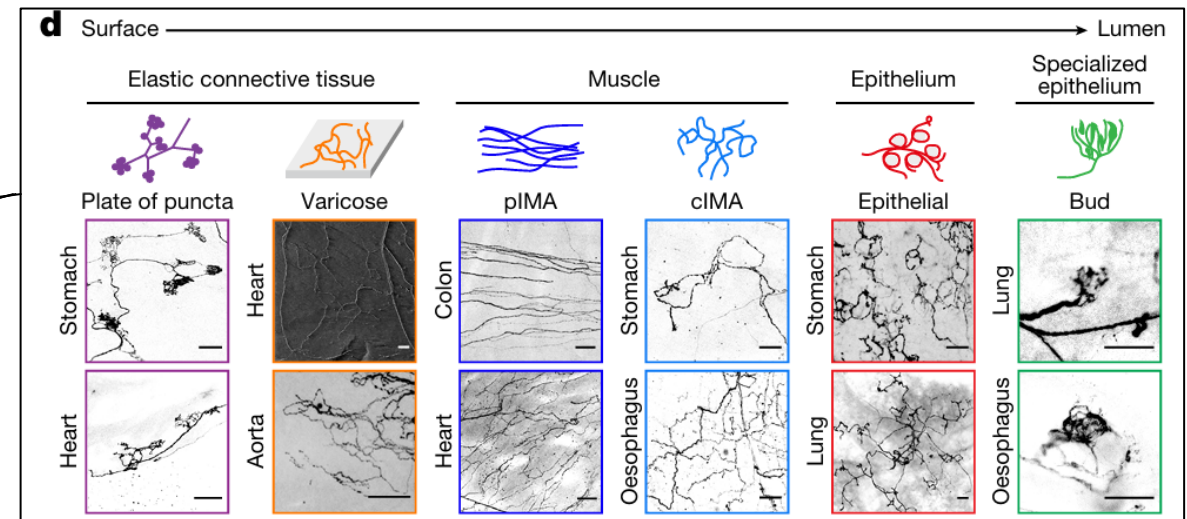
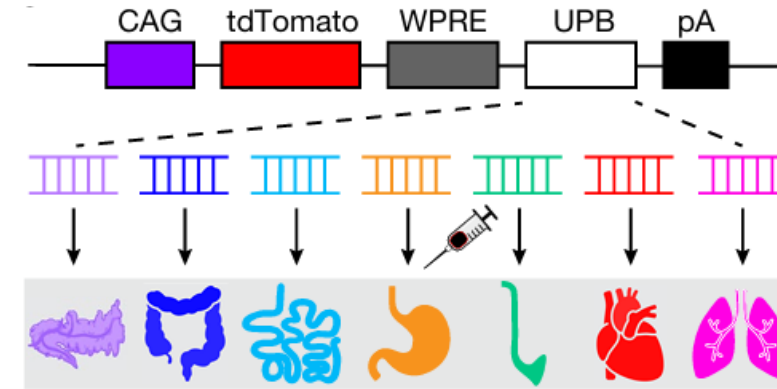
Top-down cardiac neural control governs cardiac function but underlies susceptibility to cardiac dysfunction and electrical instability.



Bottom-up neurocardiac feedback

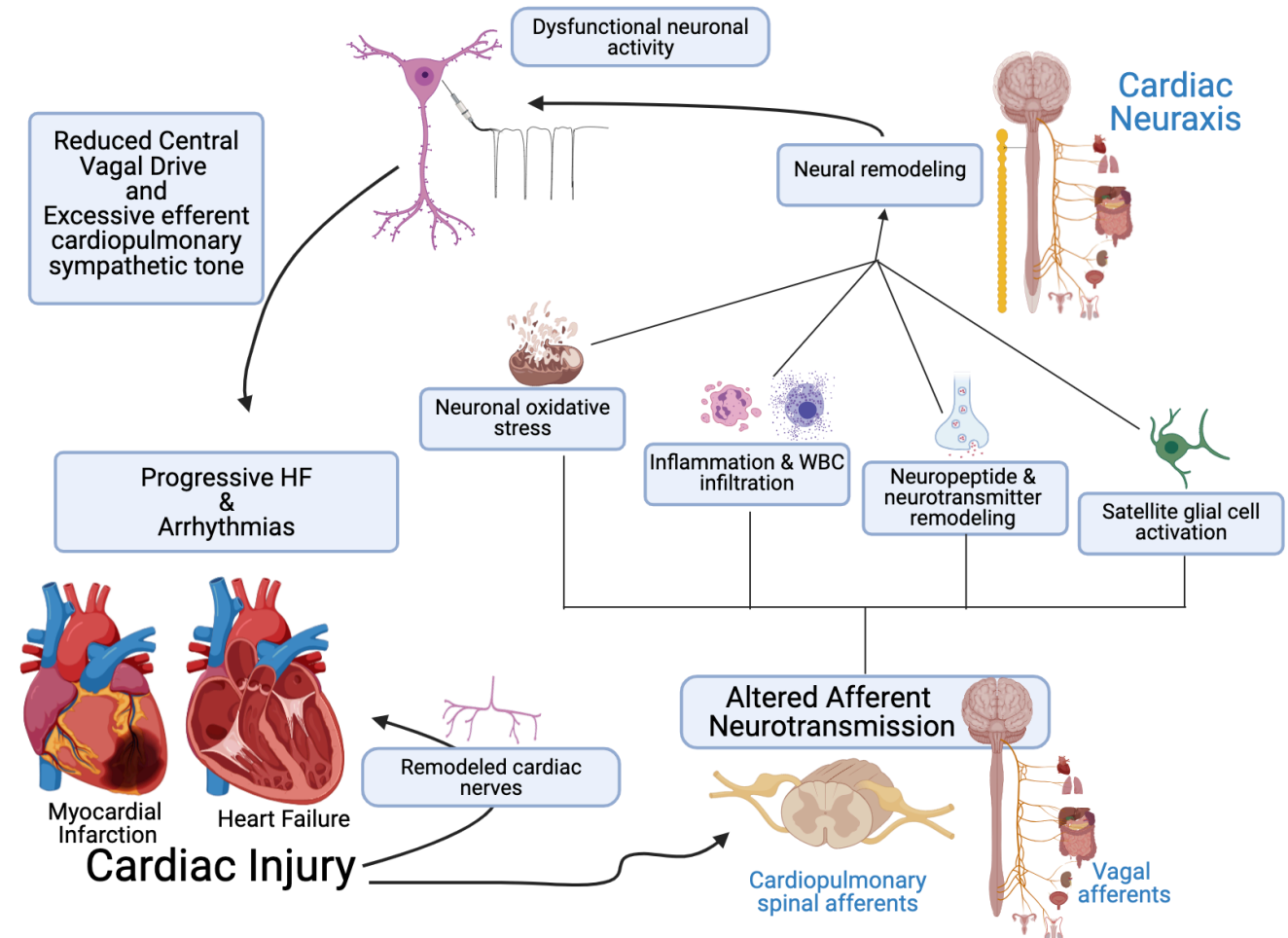


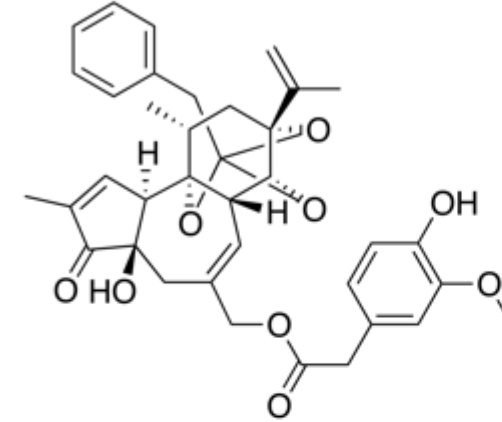
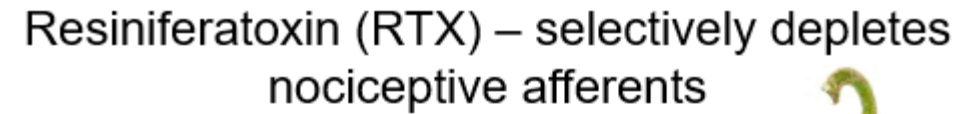
Rui Chang, PhD
Yale



Zhao et al, Nature 2022

Bottom-up neurocardiac feedback





SCOVILLE RATING	PEPPER TYPE
15 MILLION	PURE CAPSACIN
2 - 5.3MILLION	PEPPER SPRAY
1 MILLION	NAGA JOLOKIA
577,000	RED SAVINA
200000 - 350000	HABANERO
100000 - 250000	CHILTEPIN
30000 - 50000	CAYENNE
12000 - 30000	ARBOL
8000 - 23000	SERRANO
5000 - 8000	YELLOW HOT
3500 - 8000	JALAPENO
2500 - 4000	GUAJILLA
1000 - 2500	PASILLA
500 - 2000	ANAHEIM
500 - 2000	CHILE VERDE
500 - 750	RED CHILLI
0	BELL PEPPER



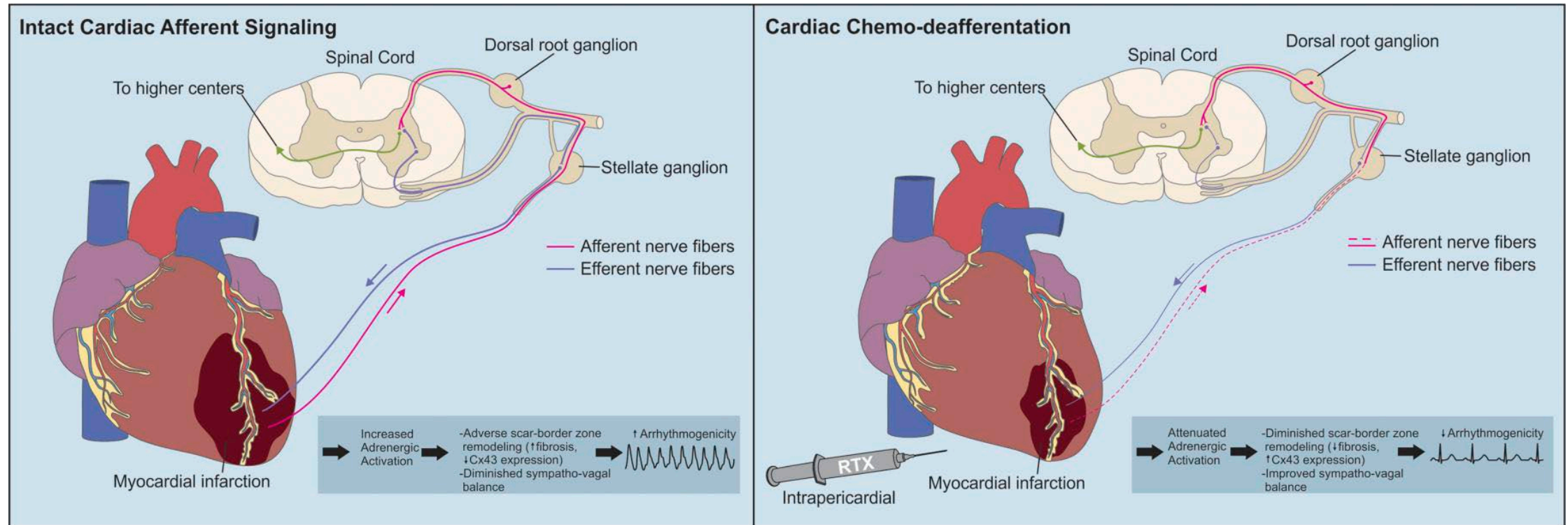
Euphorbia Poisonii



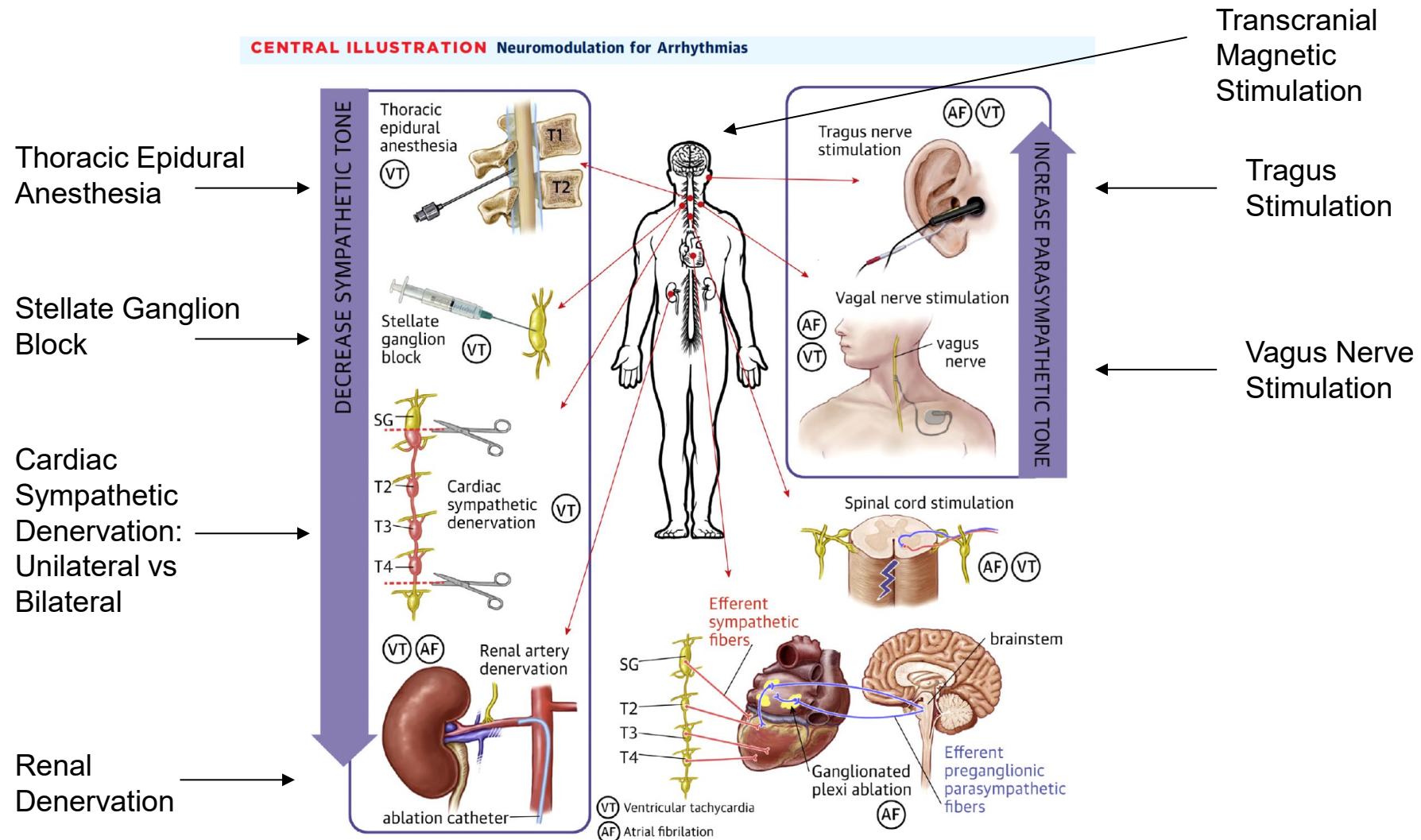
Eu Poisonii



Selective depletion of cardiac nociceptive afferent nerves limits the detrimental effects of cardiac injury e.g. myocardial infarction (heart attack)



Therapeutically targeting the brain-heart axis



Zhu, C. et al. J Am Coll Cardiol EP. 2019;5(8):881-96.

Randomized Controlled Trial > JAMA Cardiol. 2022 Apr 1;7(4):445-449.

doi: 10.1001/jamacardio.2021.6000.

Effect of Transcutaneous Magnetic Stimulation in Patients With Ventricular Tachycardia Storm: A Randomized Clinical Trial

Timothy M Markman^{1,2}, Naga Venkata K Pothineni¹, Tarek Zghaib¹, Jeffrey Smietana³, Daniel McBride⁴, Nigel A Amankwah¹, Kristin A Linn⁵, Ramanan Kumareswaran¹, Matthew Hyman¹, Jeffrey Arkles¹, Pasquale Santangeli¹, Robert D Schaller¹, Gregory E Supple¹, David S Frankel¹, Rajat Deo¹, David Lin¹, Michael P Riley¹, Andrew E Epstein^{1,6}, David J Callans¹, Francis E Marchlinski¹, Roy Hamilton^{2,7}, Saman Nazarian¹

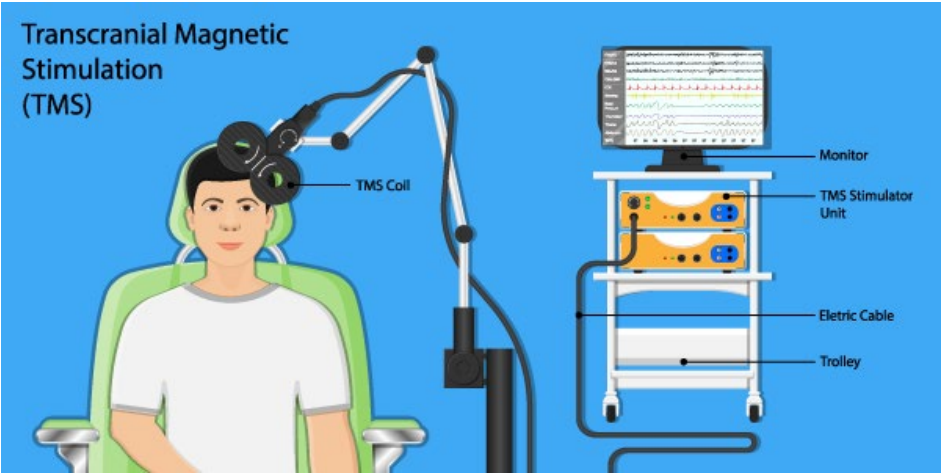
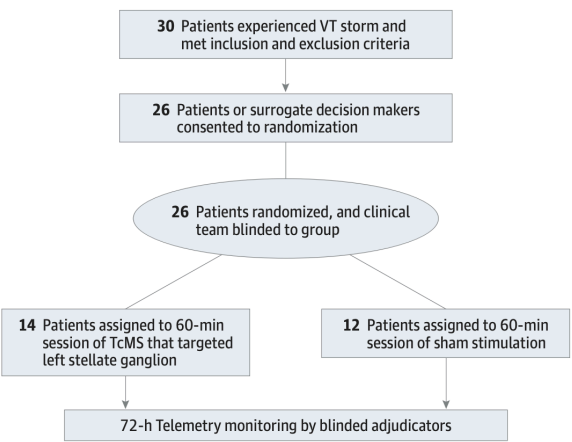
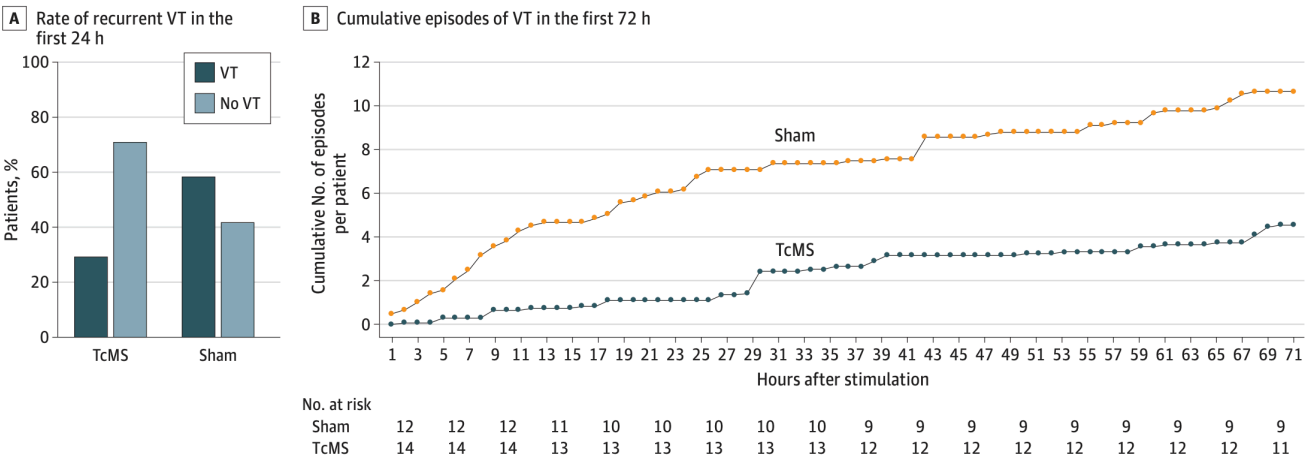


Figure 1. CONSORT Diagram



TcMS indicates transcutaneous magnetic stimulation; VT, ventricular tachycardia.

Figure 2. Recurrent Ventricular Tachycardia (VT) After Randomization

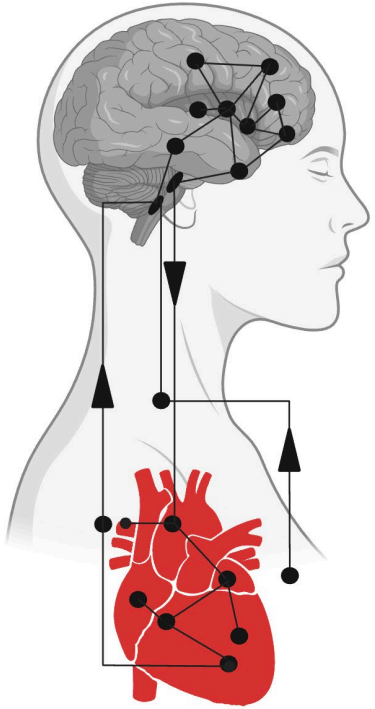




Top-down cardiac neural control governs cardiac function, but underlies susceptibility to cardiac dysfunction and electrical instability.

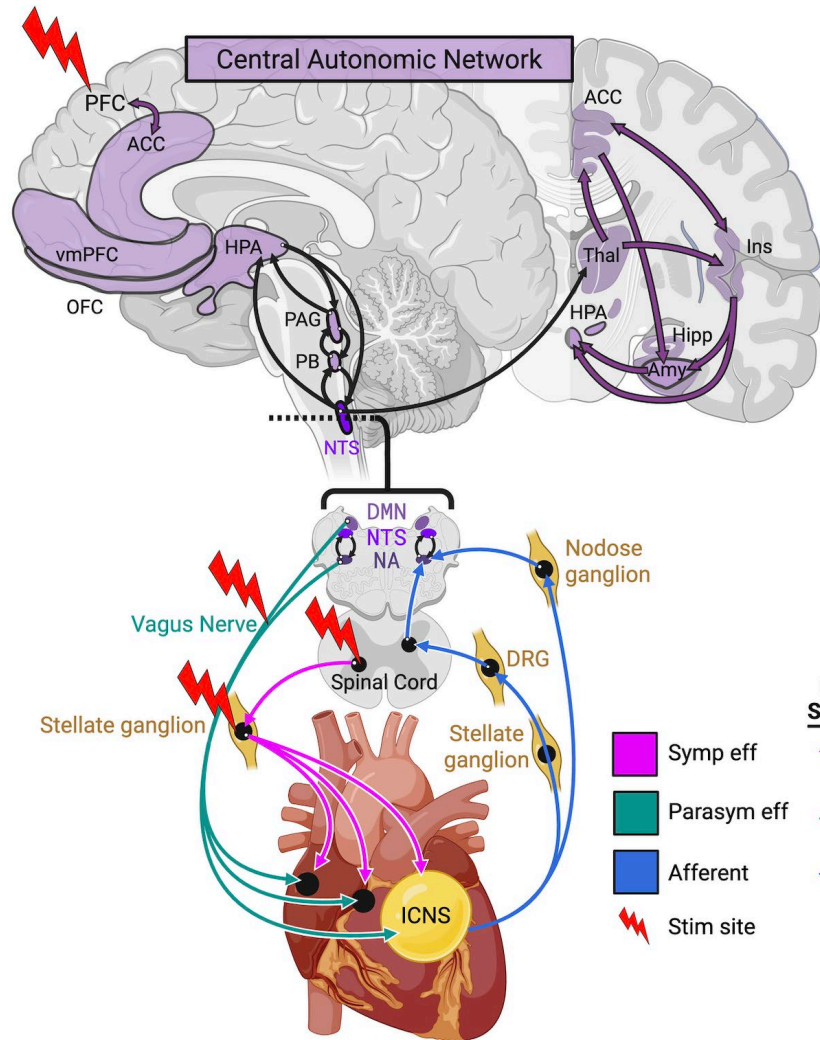
Bottom-up neurocardiac feedback is central to organ function and the pathophysiology of progressive cardiac dysfunction and heart failure.

Cardioception - The brain-heart axis and emotions



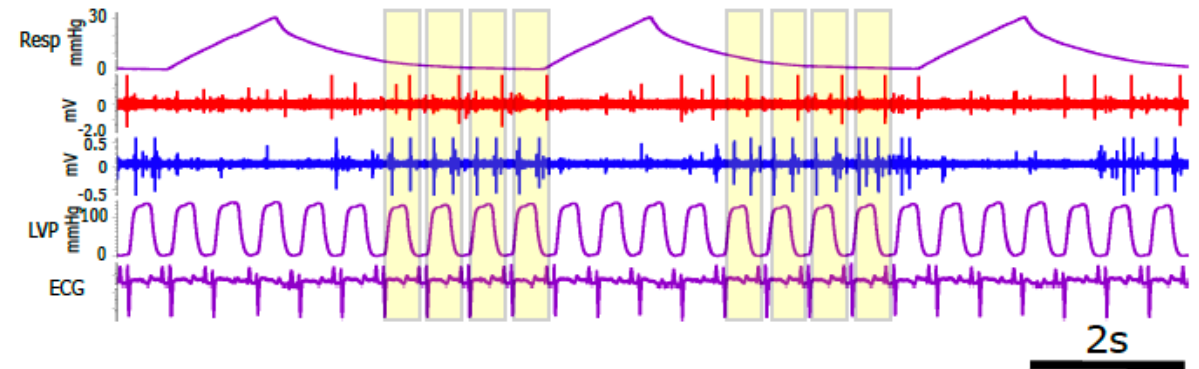
leapt heartfelt heartthrobsoul cold
sank change big hearted races
right heartsick broke kind follow warm longs rejoiced
deep full heavy take
listen cross yearned bottom open young place pounded heartstrings faint
know light sleeve goes broken gold
heartbroken heartache beat wear

The brain-heart axis and emotions - Cardioception



Talishinsky, Ajijola, Khalsa, 2025

Cardiac rhythm & mechanical function are reflected in the nervous system

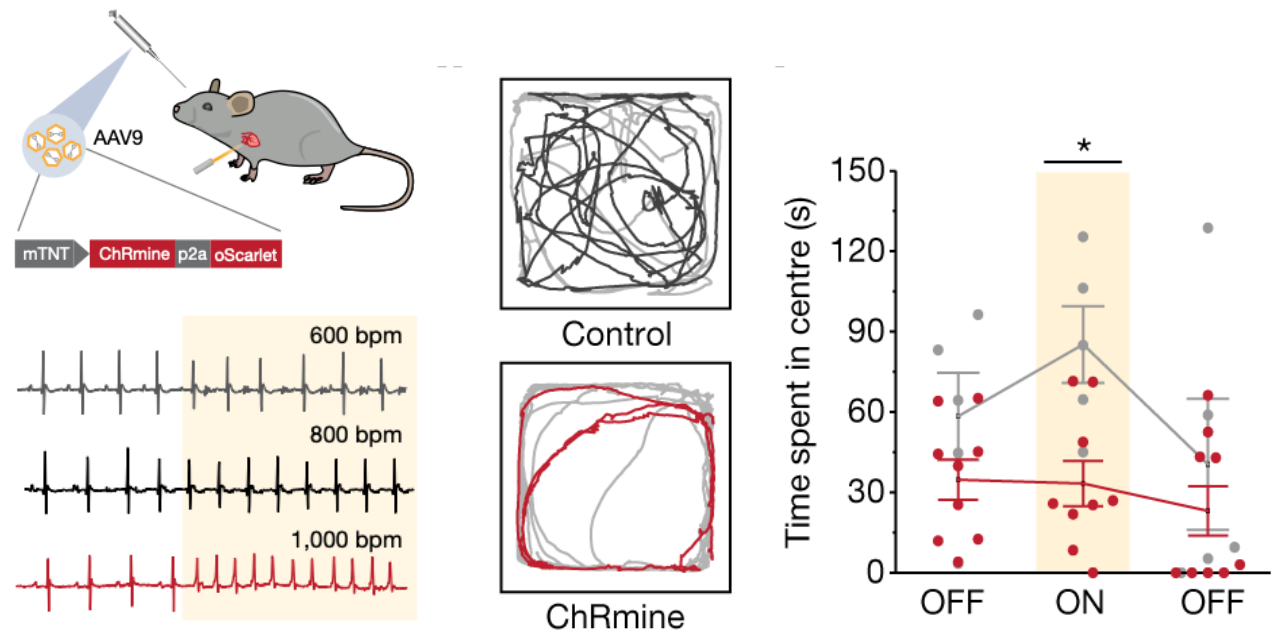


Sudarshan et al. 2021

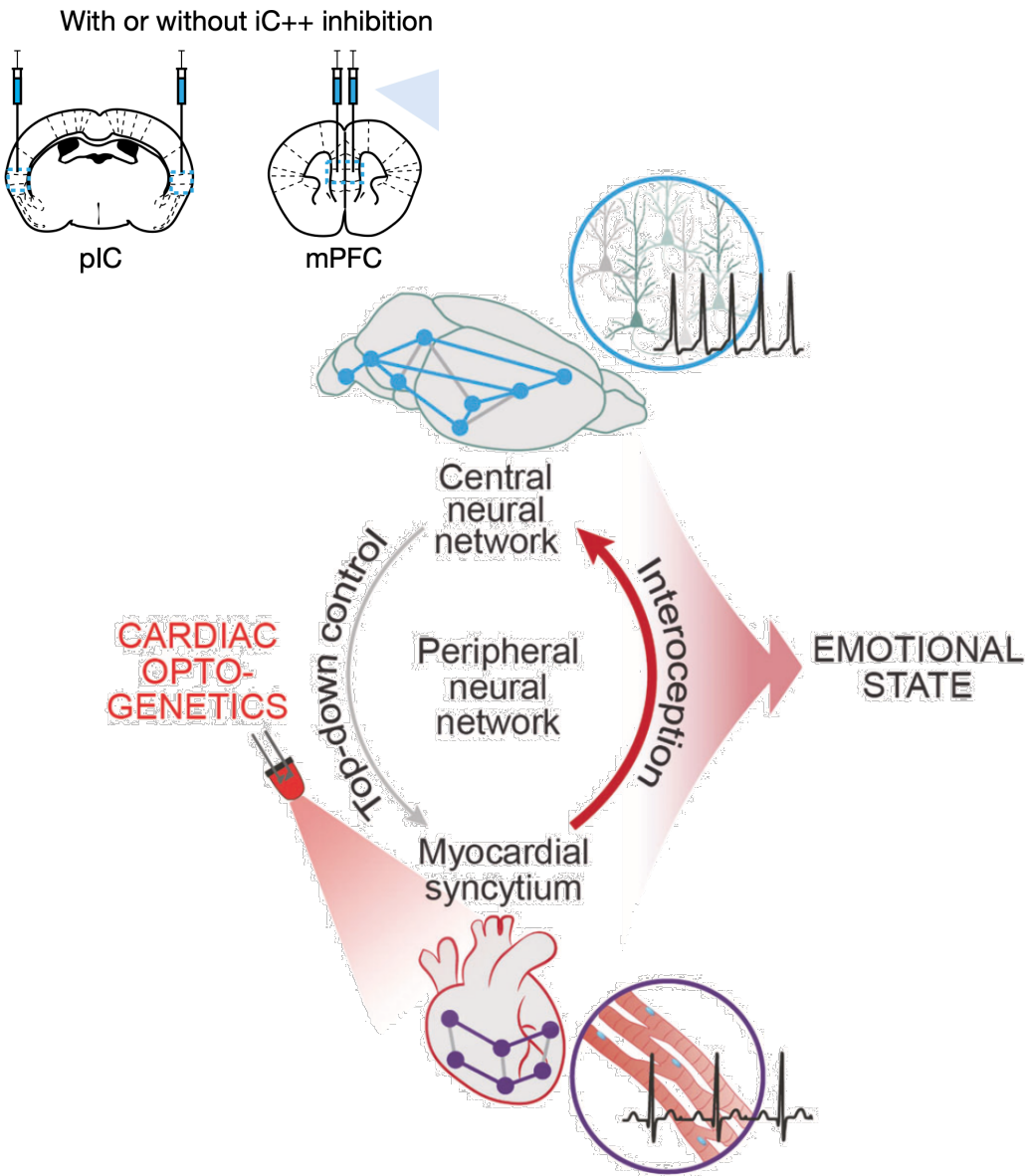
Cardiogenic control of affective behavioural state

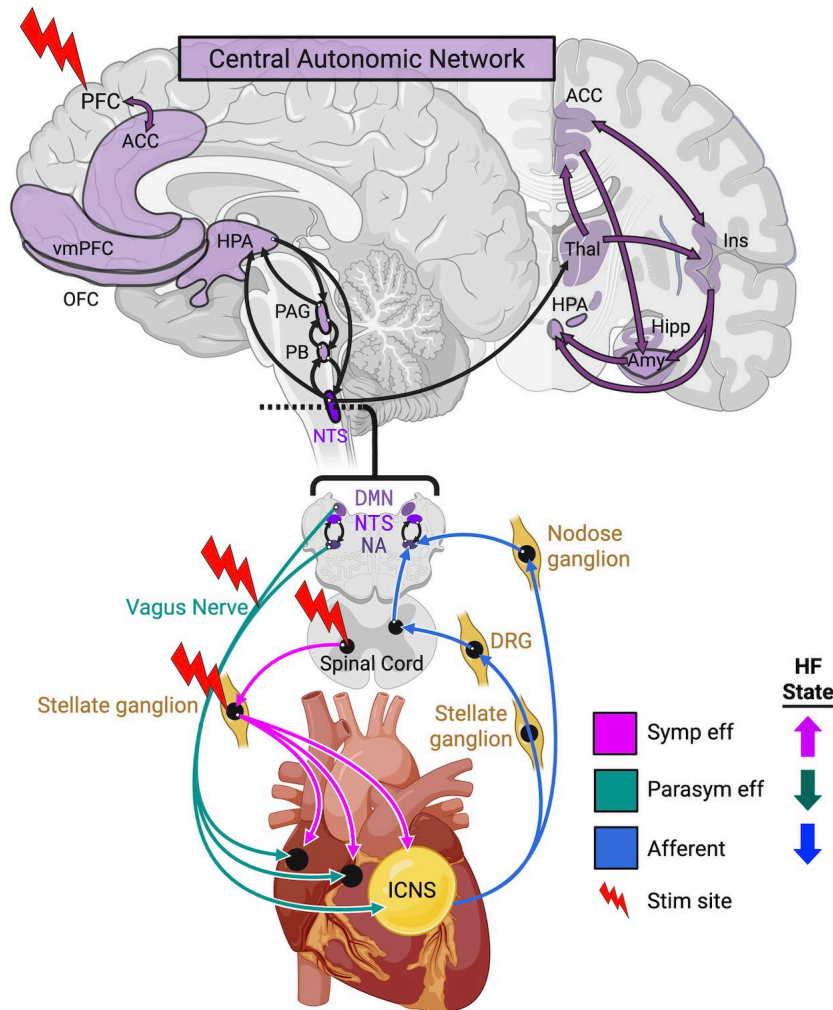
Brian Hsueh^{1,6}, Ritchie Chen^{1,6}, YoungJu Jo¹, Daniel Tang¹, Misha Raffiee¹, Yoon Seok Kim¹, Masatoshi Inoue¹, Sawyer Randles¹, Charu Ramakrishnan¹, Sneha Patel¹, Doo Kyung Kim¹, Tony X. Liu¹, Soo Hyun Kim¹, Longzhi Tan¹, Leili Mortazavi¹, Arjay Cordero¹, Jenny Shi¹, Mingming Zhao², Theodore Ho¹, Ailey Crow¹, Ai-Chi Wang Yoo¹, Cephra Raja¹, Kathryn Evans¹, Daniel Bernstein², Michael Zeineh³, Maged Goubran³ & Karl Deisseroth^{1,4,5}✉

Nature | 2023



“We identified the posterior insular cortex as a potential mediator of bottom-up cardiac interoceptive processing, and found that optogenetic inhibition of this brain region attenuated the anxiety-like behavior that was induced by optical cardiac pacing.”





Top-down cardiac neural control governs cardiac function but underlies susceptibility to cardiac dysfunction and electrical instability.

Bottom-up neurocardiac feedback is central to organ function and the pathophysiology of progressive cardiac dysfunction and heart failure.

Cardiac interoceptive mechanisms influence brain-wide circuits that govern affective states and behavior.

Fundamental Research

Governance of brain-body homeostasis.

Mechanisms of neural dysfunction following organ injury.

Diagnostic/Biomarkers

Measures of optimal homeostasis.

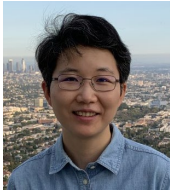
Causal drivers, predictors and biomarkers of maladaptive brain-body interactions.

Therapeutics

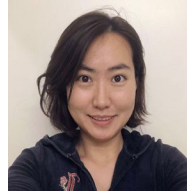
Treatments to modulate CNS and PNS circuits for brain and organ health, using non- or minimally-invasive approaches.

Prevention of aberrant brain-body interactions to improve health.

Our Team



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Misale Mesfin



Joey Ettipio



Christian Miccile



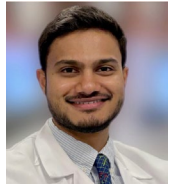
John Odeh



Nhi Doan



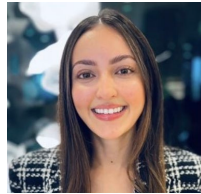
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Zixi "Jack" Cheng (UCF)

Thank You

