



University of California
San Francisco

Deep Brain Stimulation for Chronic Pain

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Pain as the 5th vital sign?



But there is no objective measure of pain!

Can we build a K3 indicator?



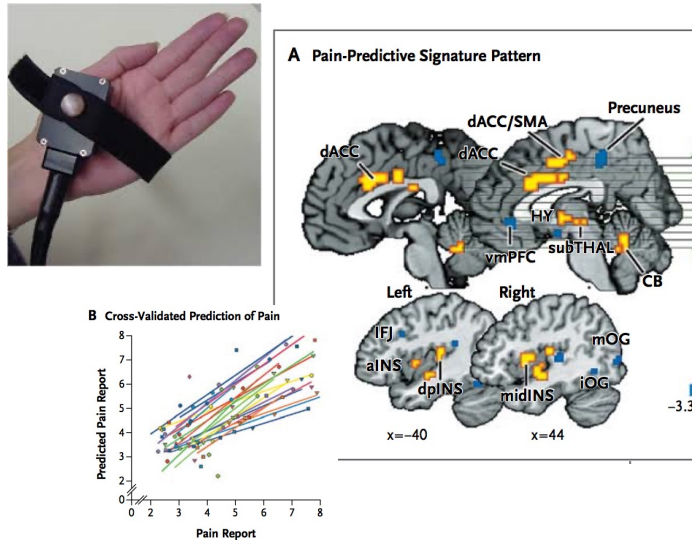
Credit: memory-alpha.fandom.com

USF

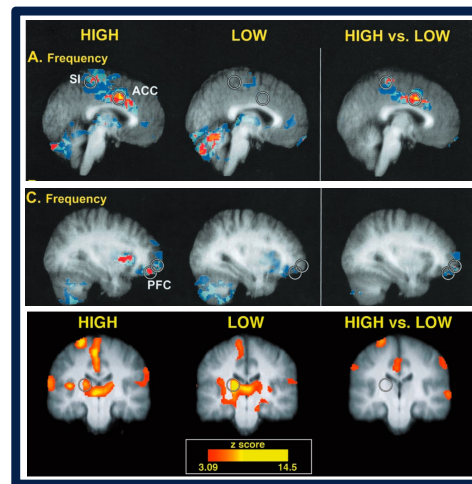
Pain is in the BRAIN.

But, prior evidence is mostly from experiments on healthy people in the lab.

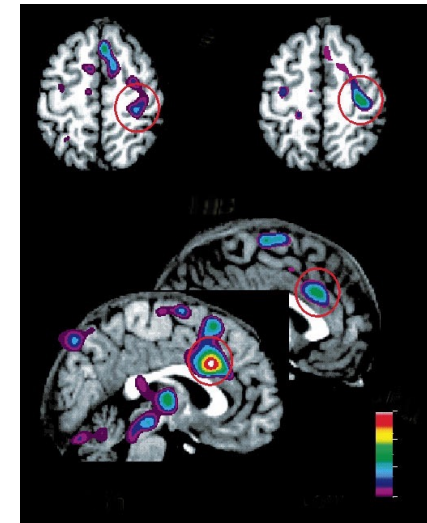
Heat pain testing



Wager et al., NEJM 2013

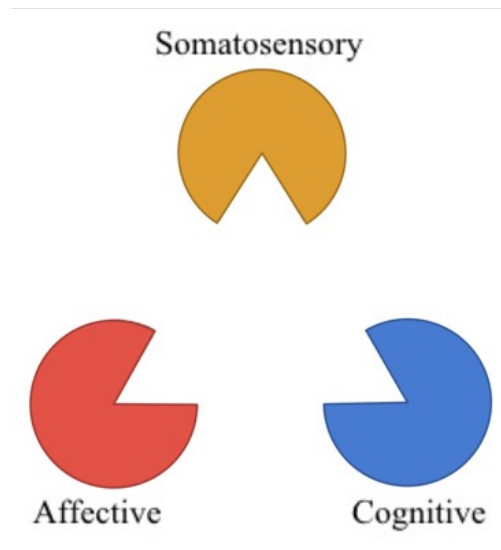


Coghill et al., PNAS 2003

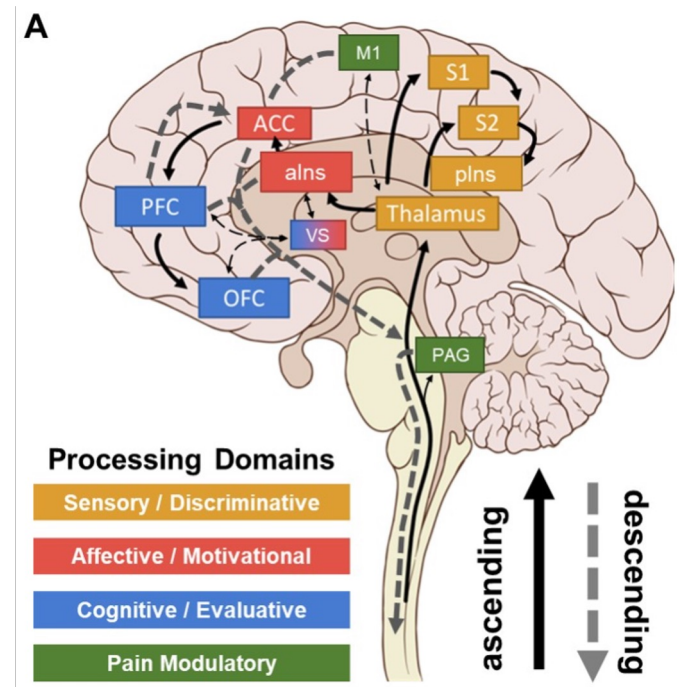


Rainville et al., Science 1997

Chronic Pain Has Multiple Dimensions distributed brain-wide



Inspired by Melzack and Wall (1965)



Motzkin J, Kanungo I, et. al., *Frontiers in Pain Research*, 2023

Brain stimulation for pain over the years...

Stimulation of internal capsule for relief of chronic pain

JOHN E. ADAMS, M.S., YOSHIO HOSOBUCHI, M.D.,
AND HOWARD L. FIELDS, M.D.

Departments of Neurological Surgery and Neurology, University of California
School of Medicine, San Francisco, California

Mazars et al.
(France)

1960

1974

1973

1992,
1998

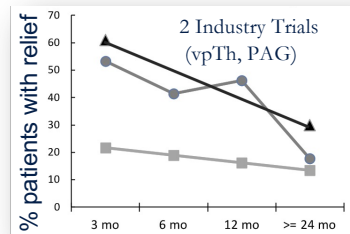
2014

2017

Chronic Thalamic Stimulation for the
Control of Facial Anesthesia Dolōrosa

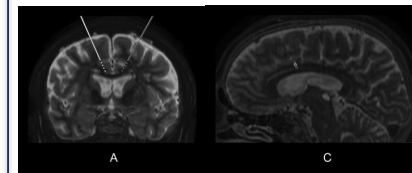
Yoshio Hosobuchi, MD; John E. Adams, MD; Burt Rutkin, MS,

From the Department of Neurological Surgery, University of California, School of Medicine, San Francisco.

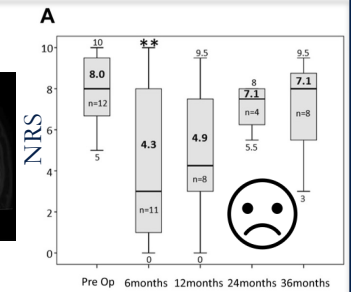


Coffey et al., 2011
Levy et al., 1986

ACC



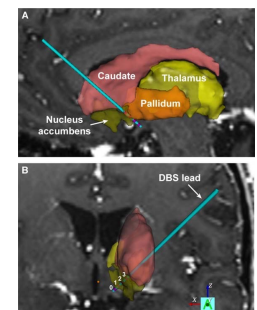
Boccard et al., 2014, 2017



Randomized Clinical Trial of Deep Brain
Stimulation for Poststroke Pain

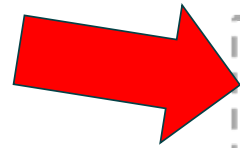
Good for depression
Bad for pain

Lempka et al., Ann. Neurol. 2017



Our Solution / Goal:

Can we
identify
chronic pain
biomarkers?



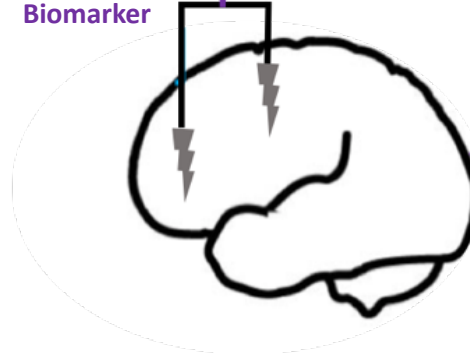
Closed-Loop Controller

Pain State
Decoder

Feedback
Controller

Feedback:
Neural State
Biomarker

State dependent
stimulation



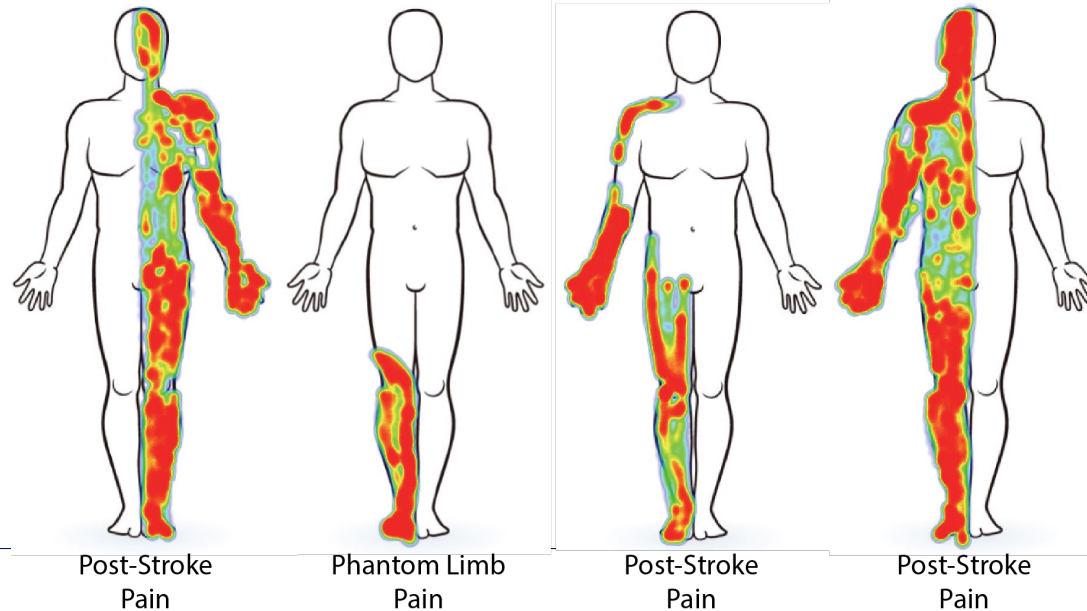
First-in-human prediction of chronic pain state using intracranial neural biomarkers

Received: 13 April 2021

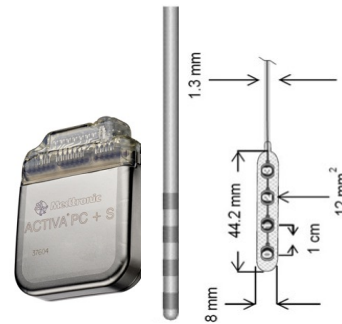
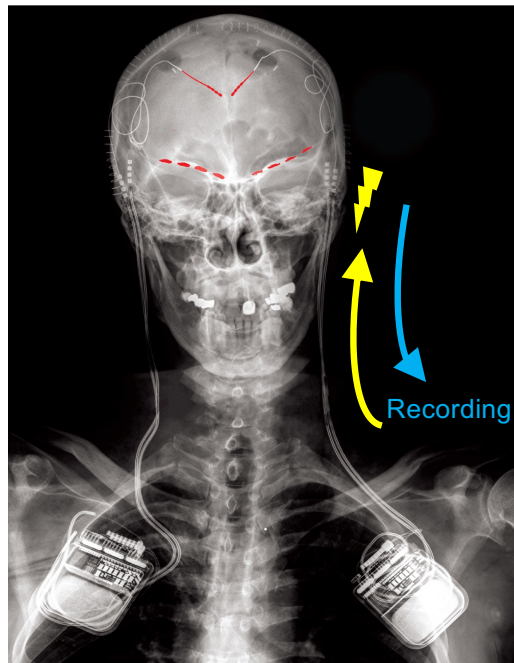
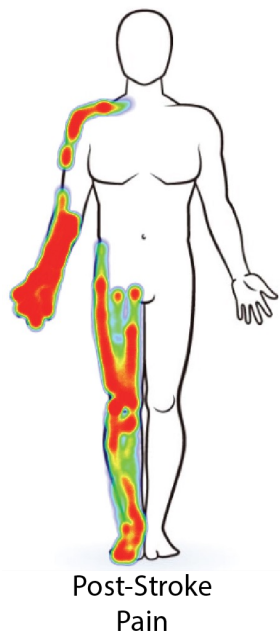
Accepted: 18 April 2023

Published online: 22 May 2023

Prasad Shirvalkar^{1,2,3,4}✉, Jordan Prosky^{3,4}, Gregory Chin³,
Parima Ahmadipour⁵, Omid G. Sani⁵, Maansi Desai⁵, Ashlyn Schmitgen^{3,4},
Heather Dawes^{3,4}, Maryam M. Shanechi⁵, Philip A. Starr^{3,4,7} &
Edward F. Chang^{3,4,7}

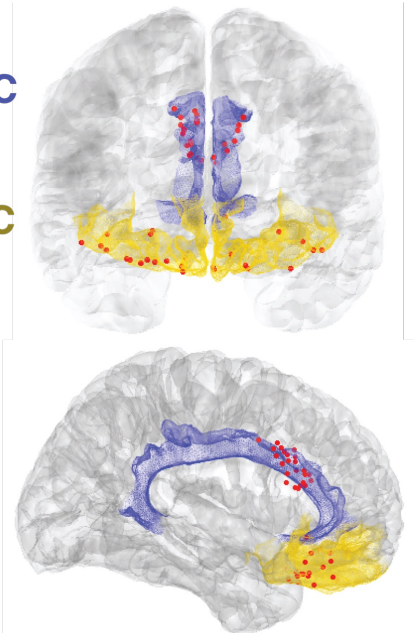


Electrode implants in the brain allow us to monitor and modulate brain signals at-home.

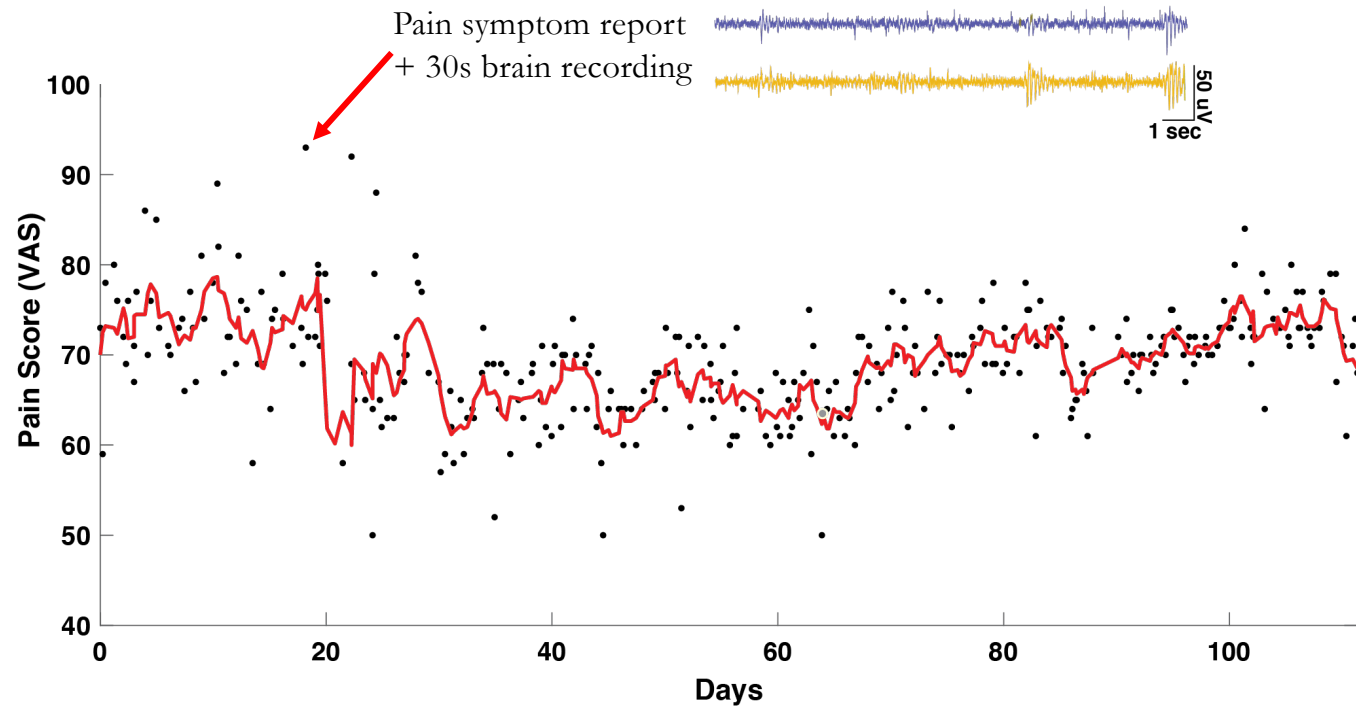
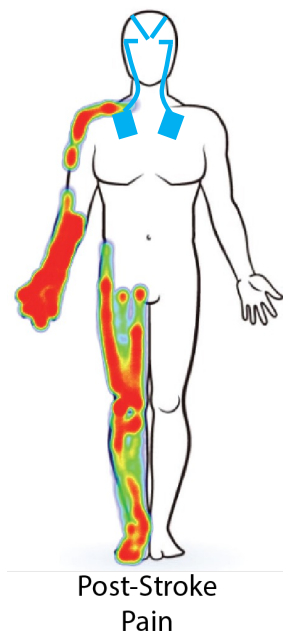


ACC

OFC

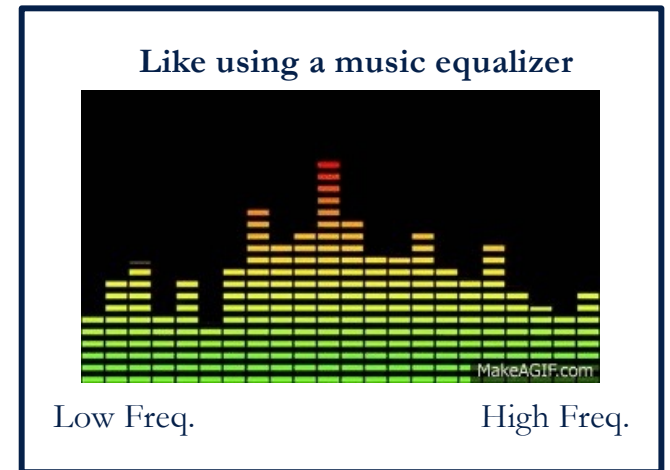
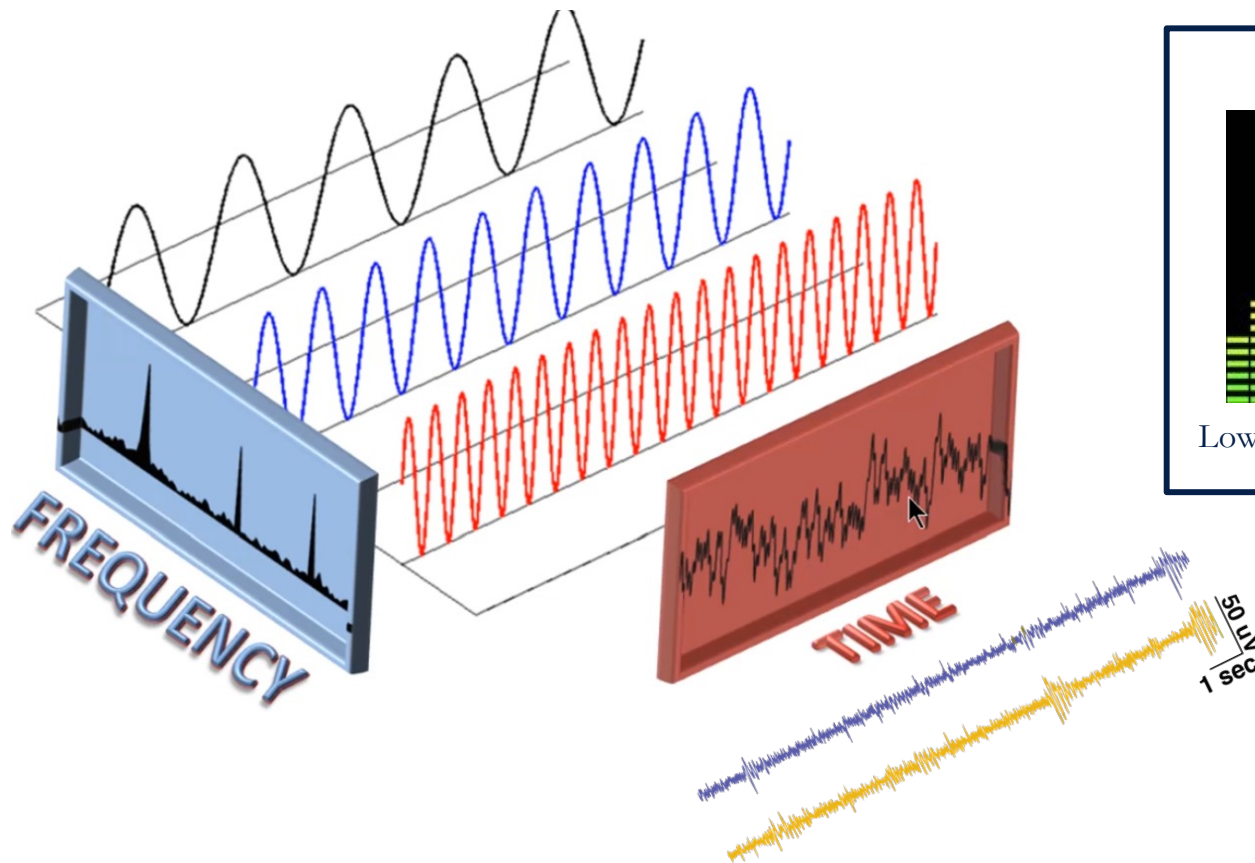


At-home measurements of real-world chronic pain symptoms and brain signals

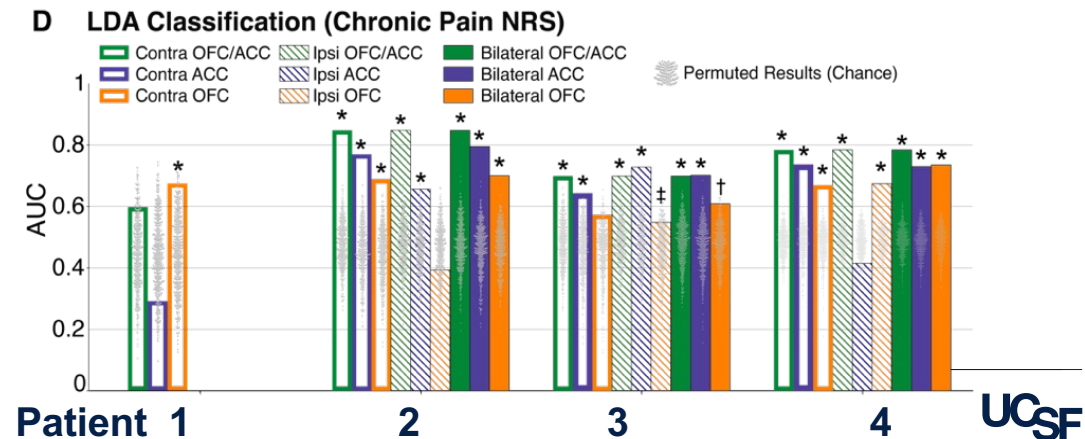
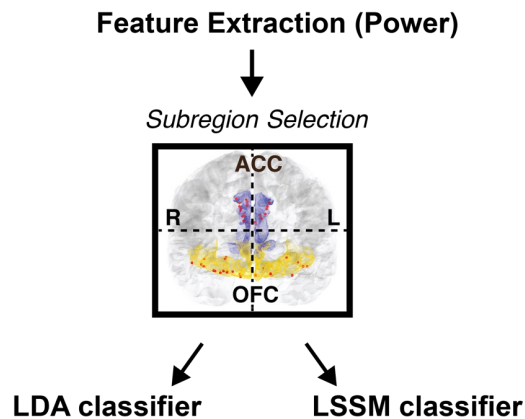
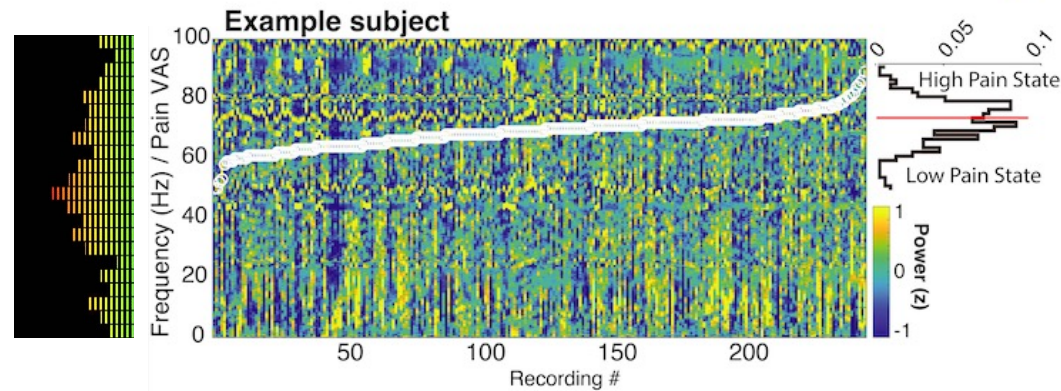


Shirvalkar et al.
2023 *Nat Neuro*

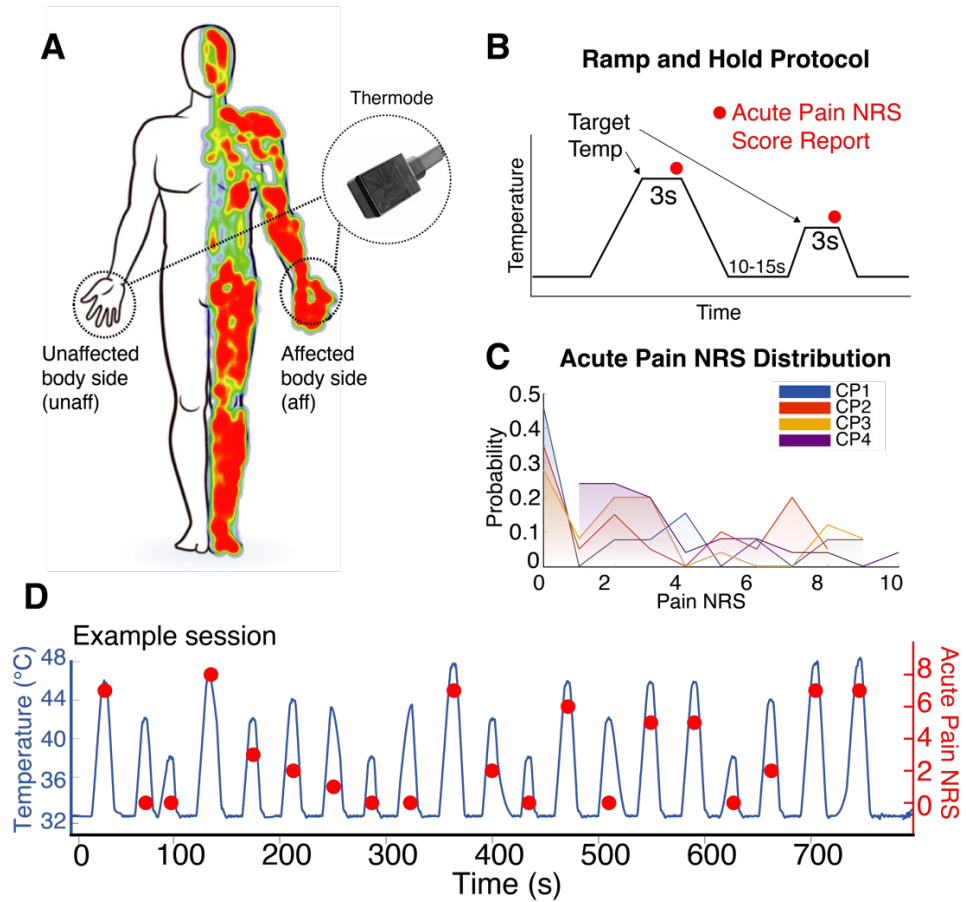
Analyzing Brain Signal Frequency Components



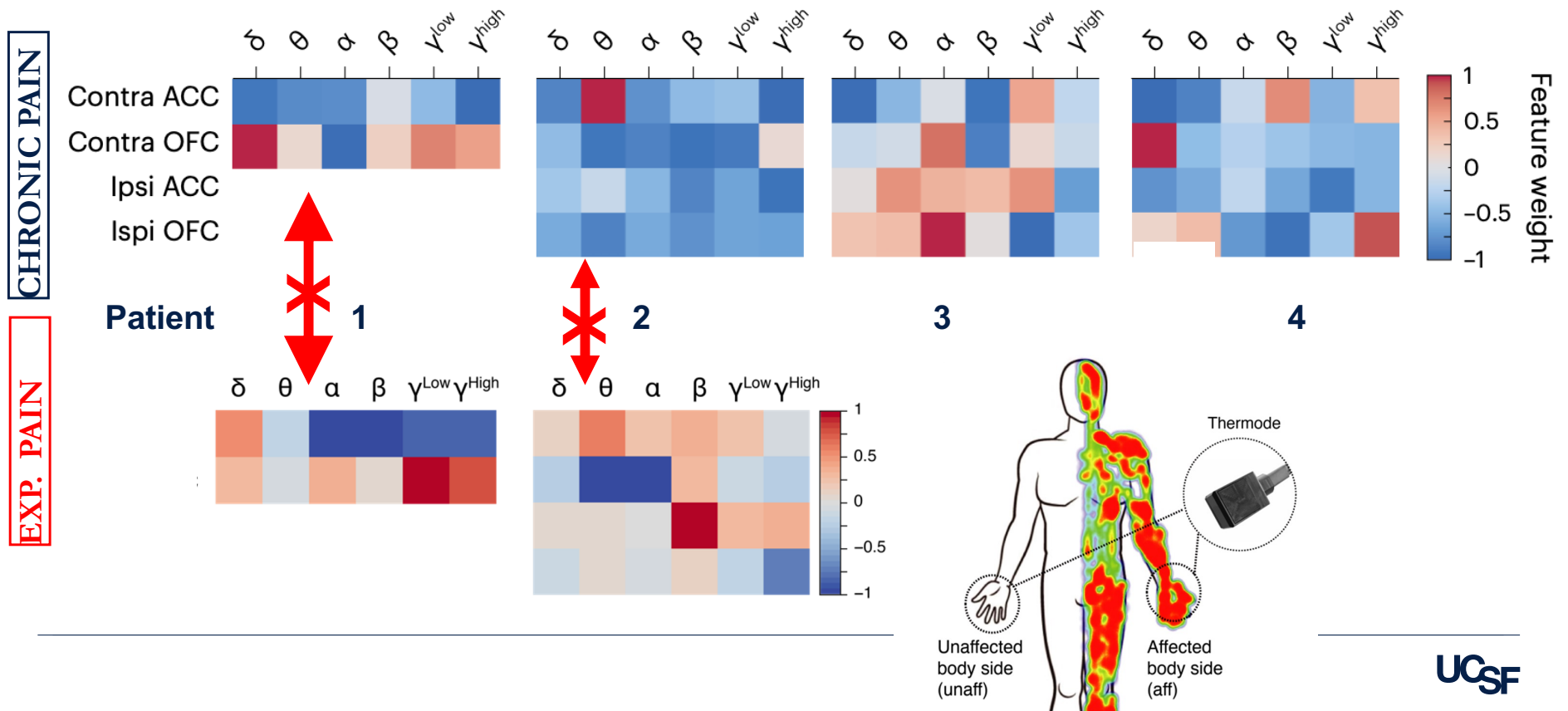
Direct brain signal measurements can track real-world pain severity



What about experimental pain?



Brain signatures of pain showed intra-individual variability. Chronic Pain \neq Experimental Pain.

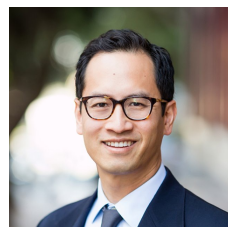




Thank you!

• Patients Living with Chronic Pain

- Heather Dawes, PhD
- Howard Fields, MD, PhD
- Andrew Krystal, MD, PhD
- Niko Schiff, MD
- Vikram Rao, MD PhD
- Daniel Lu MD, PhD
- Cynthia Kubu, PhD
- Joshua Kuluva, MD



Edward Chang, MD
Co-investigator



Philip Starr, MD, PhD
Co-investigator



Julian Motzkin, MD, PhD



Chad Sitgraves, MS



Joanna Lin

UF-Gainesville

- Cora DeHemptinne, PhD
- Jackson Cagle, PhD

USC

- Omid G. Sani, PhD
- Parima Ahmadipour
- Maryam M. Shanechi, PhD

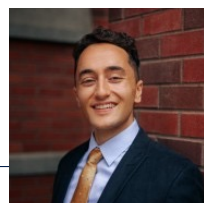
**NIH
HEAL
INITIATIVE**



Ishan Kanungo
MD candidate



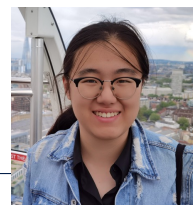
Jeremy Saal
PhD candidate



Ryan Leriche



Andreea Seritan, MD
Psychiatrist



Yiyuan Han, PhD

UCSF

University of California
San Francisco