UNIVERSITY OF MICHIGAN

Brain as a Research and Therapeutic Target for Chronic TMD

Neuroscience Driven Tech-Innovations from the Lab to the Clinic

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Molecular & Behavioral Neuroscience Institute
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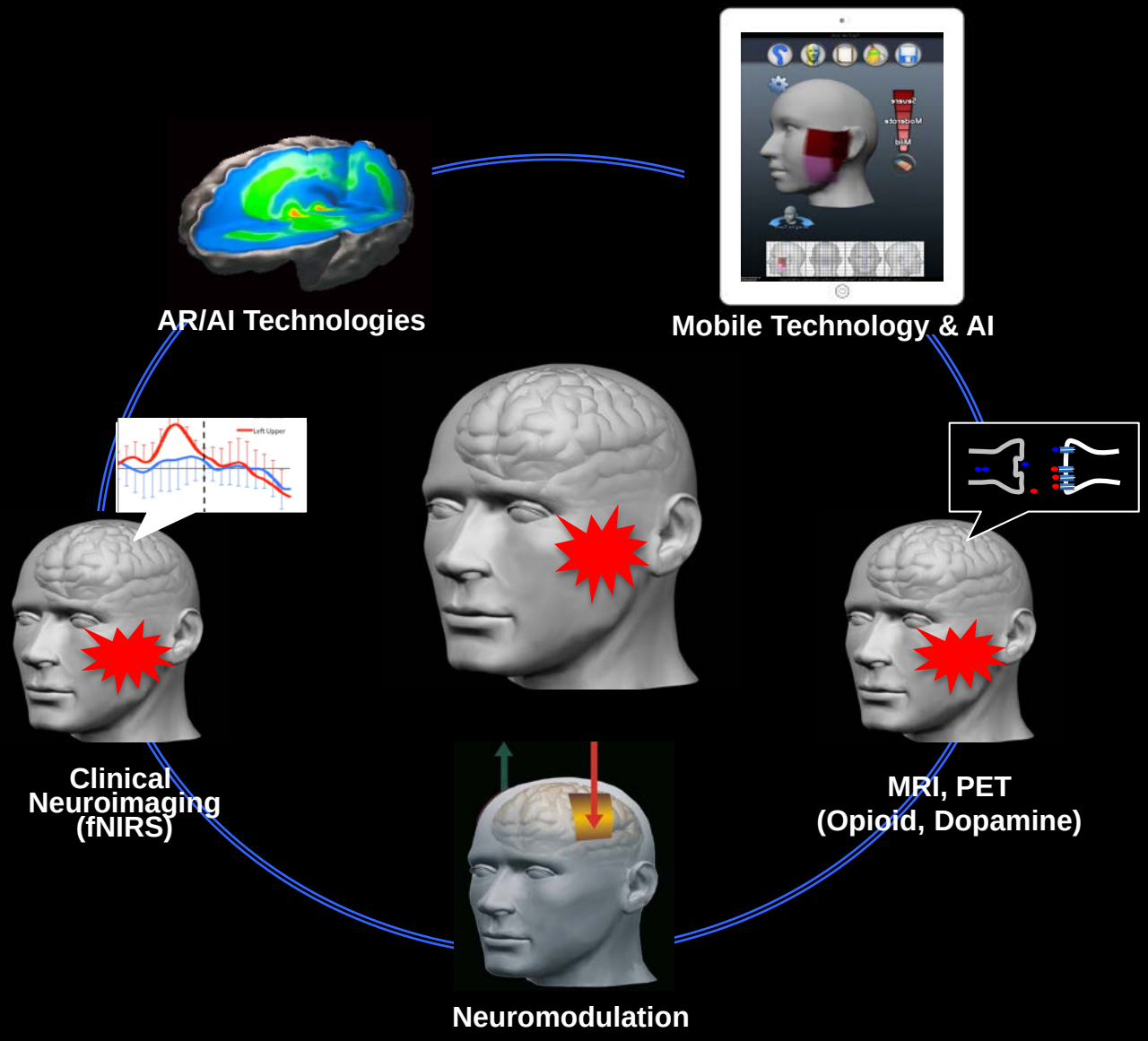
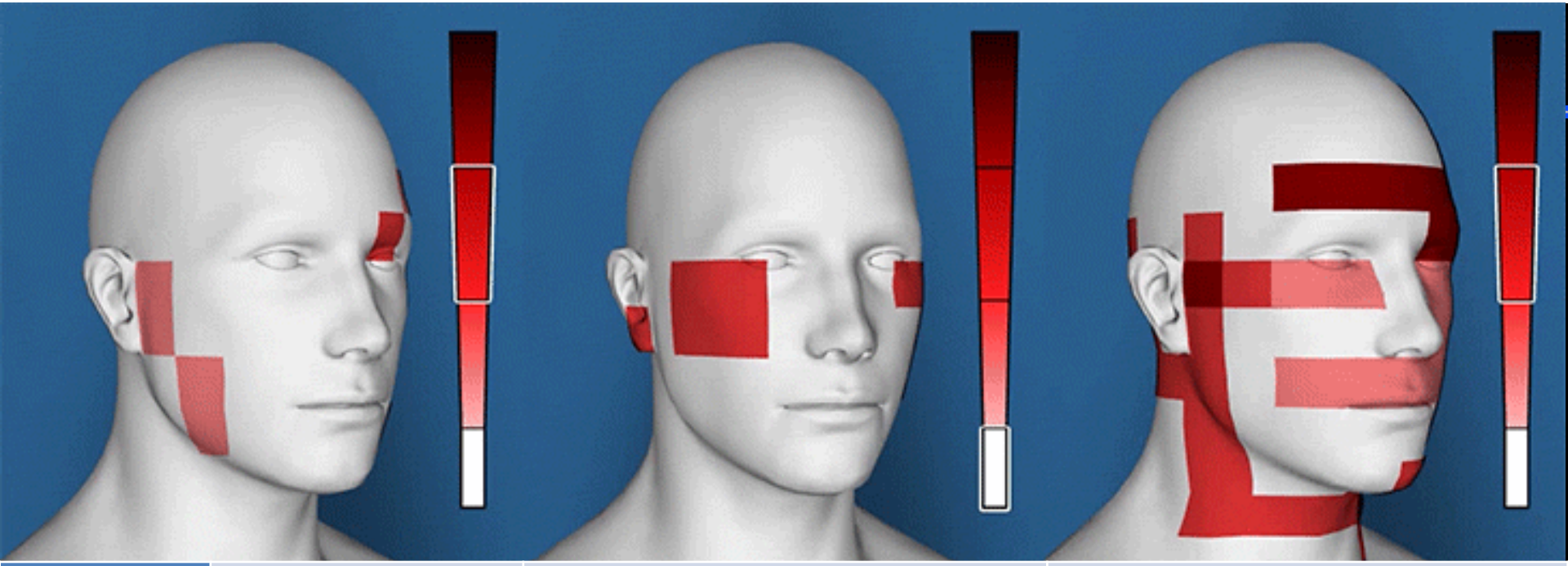
CHGD

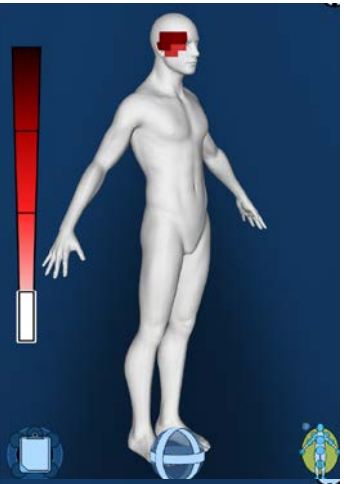
Disclosure: MoxyTech LLC
(Co-Founder and Chief Science Officer)

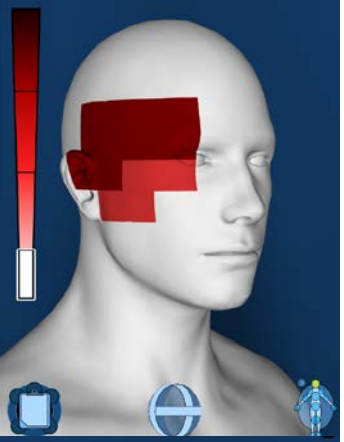

AR/AI Technologies
Mobile Technology & AI
Clinical
Neuroimaging
(fNIRS)
MRI, PET
(Opioid, Dopamine)
Neuromodulation

What are we measuring?

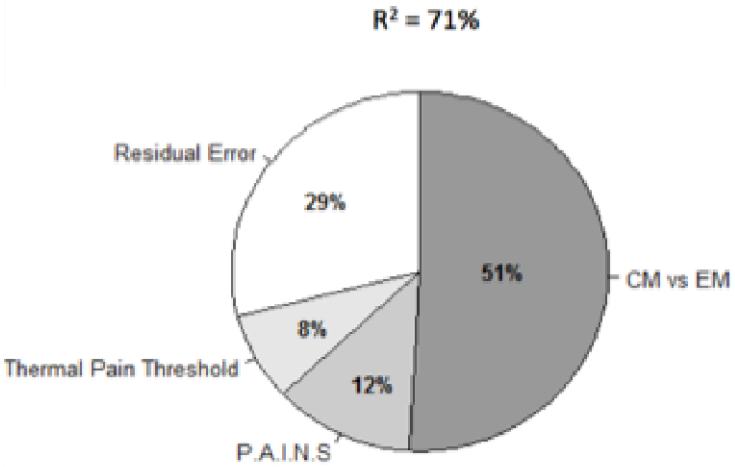


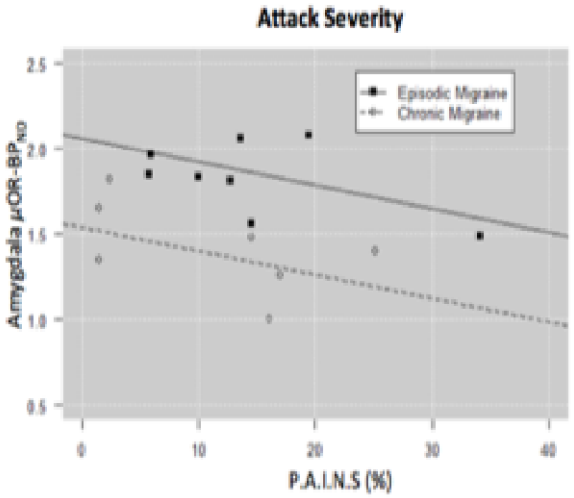
VAS	5.9	6.3	5.7
GeoPain Average	1.4	2.0	2.1
Area	7.3%	5.5%	36.4%
P.A.I.N.S.	3.5%	3.6%	25.7%



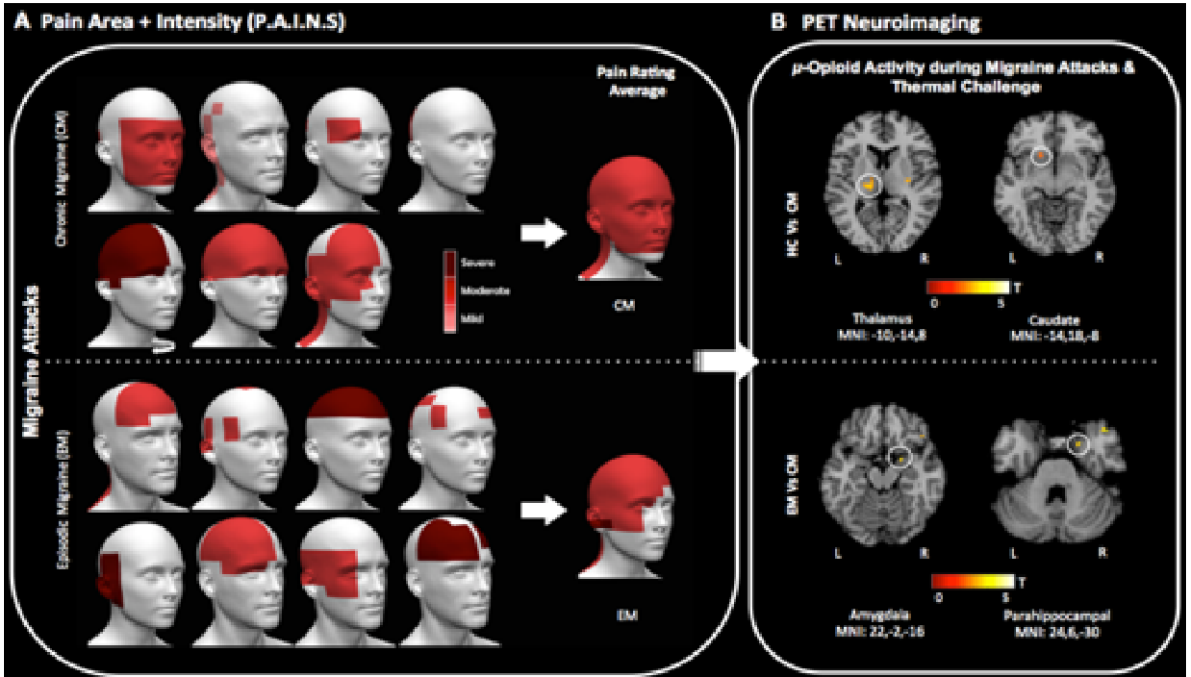


Migraine Severity (P.A.I.N.S.) and Endogenous μ-Opioid Activity

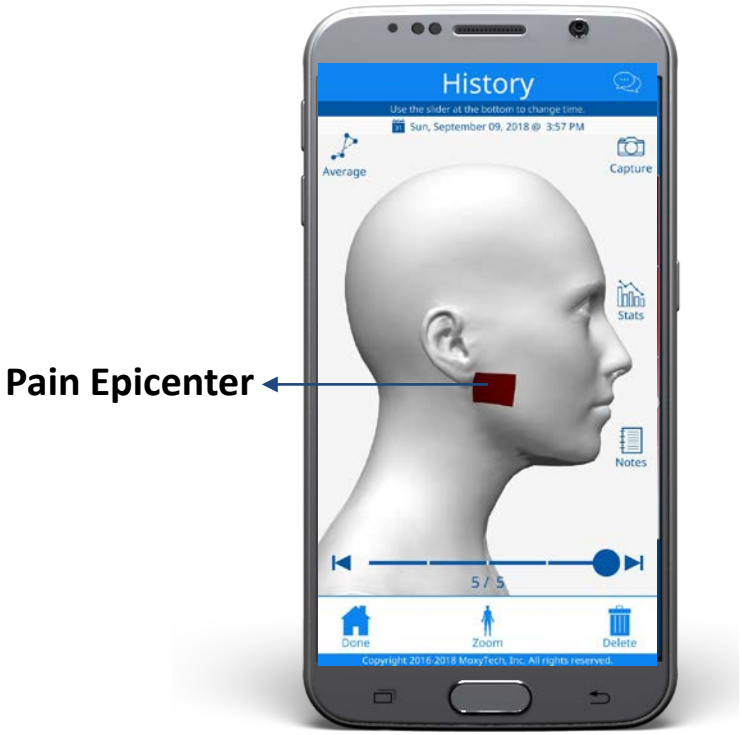


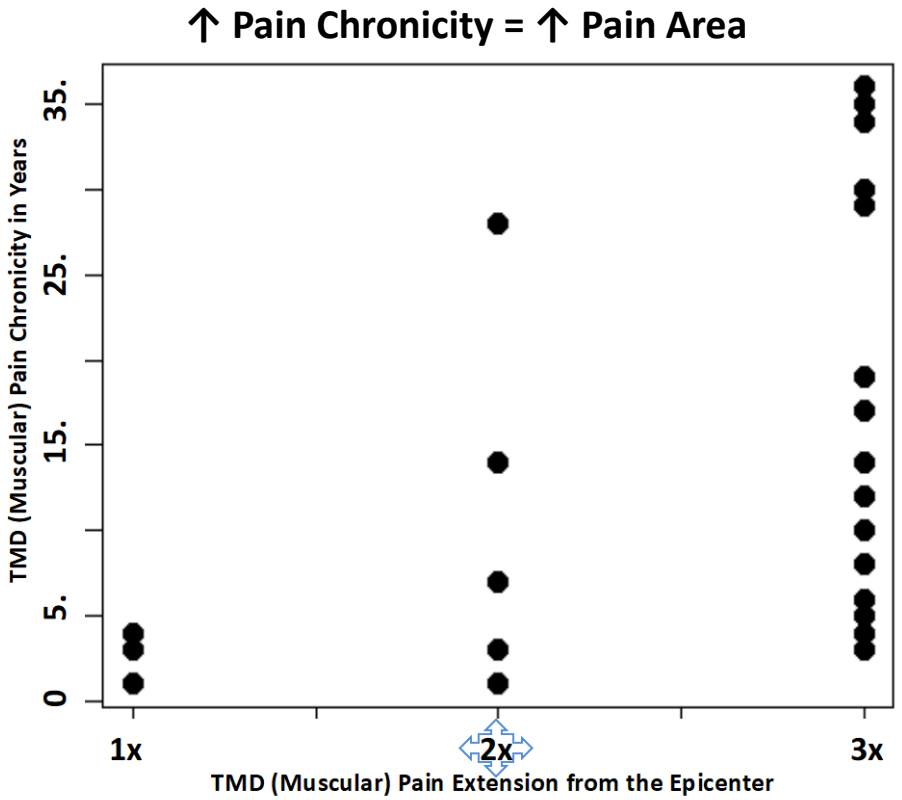


↑ Attack Pain Area + Intensity (P.A.I.N.S.) = ↓ μ-Opioid Receptor Availability



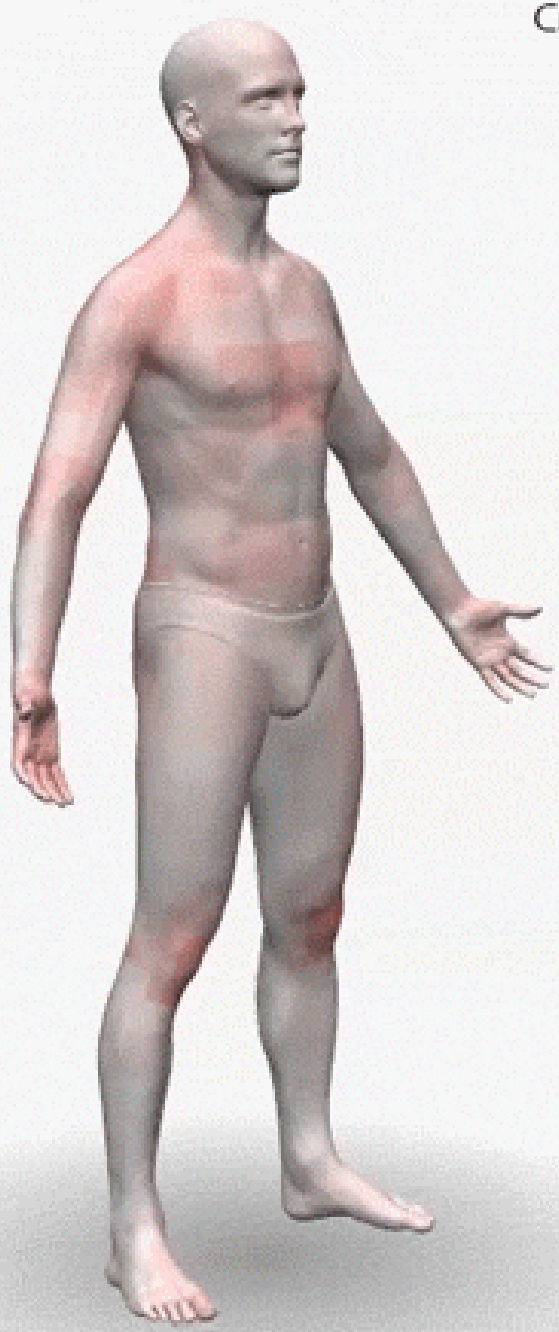
TMD Chronicity and Pain Area

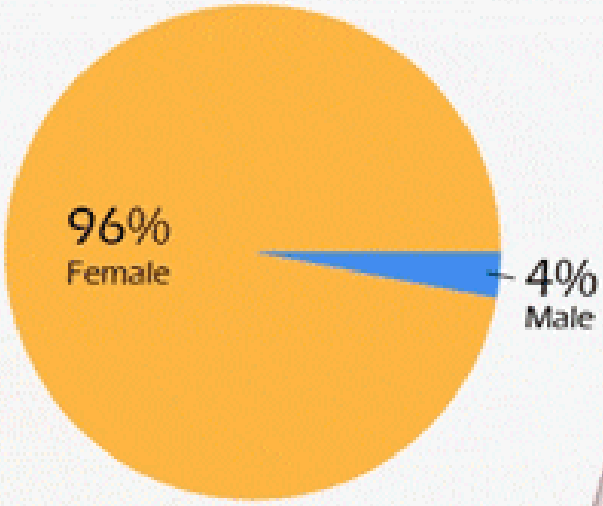


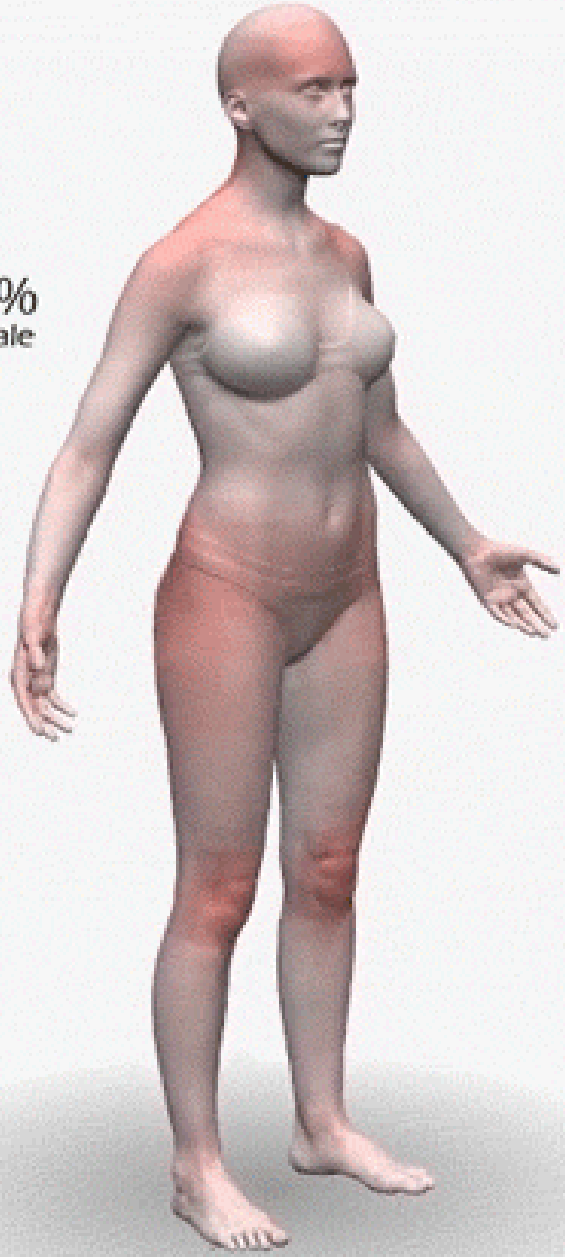


Average of Pain - Fibromyalgia

Created from users of GeoPain







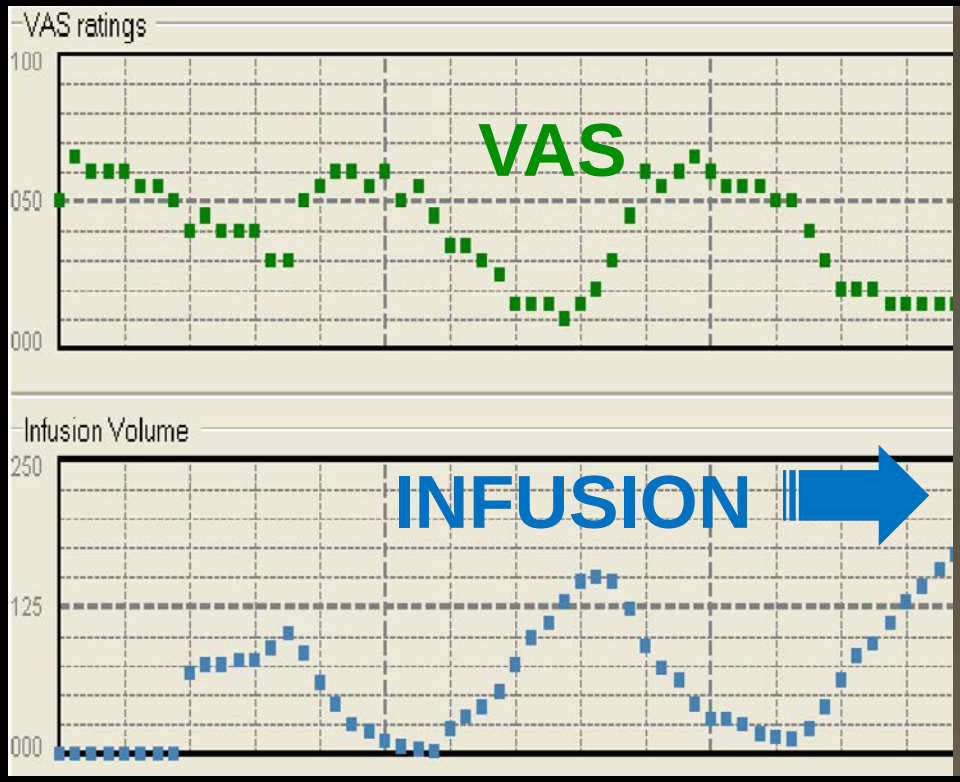
GeoPain™

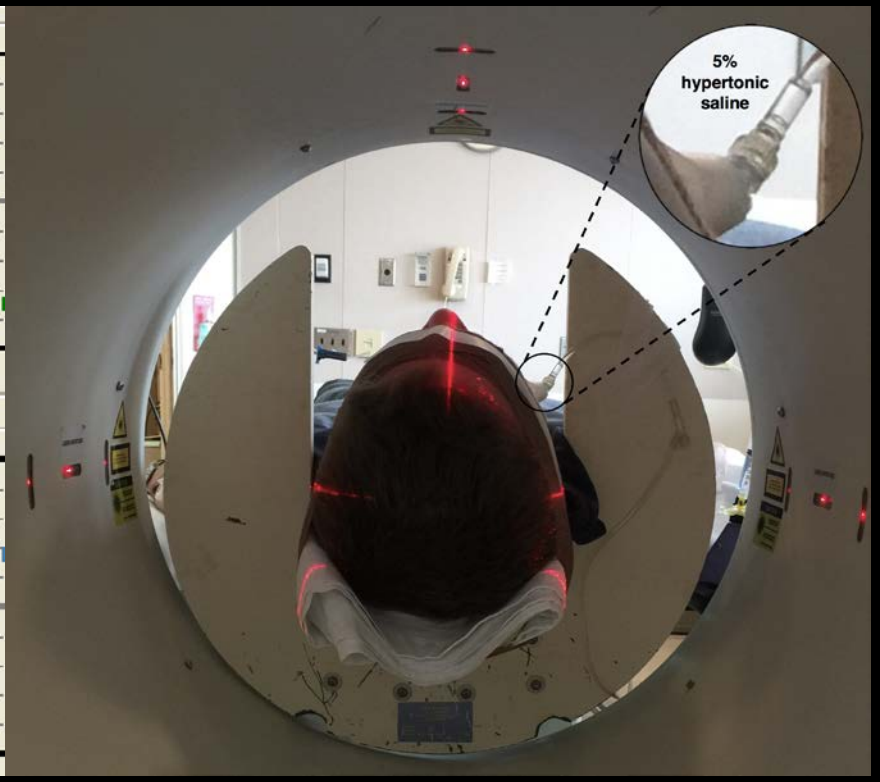
Bringing Precision to Pain Care

www.geopain.com

Chronic TMD
&
Mu-Opioid Activity

Sustained Masseteric Pain Threshold (SMPT) challenge





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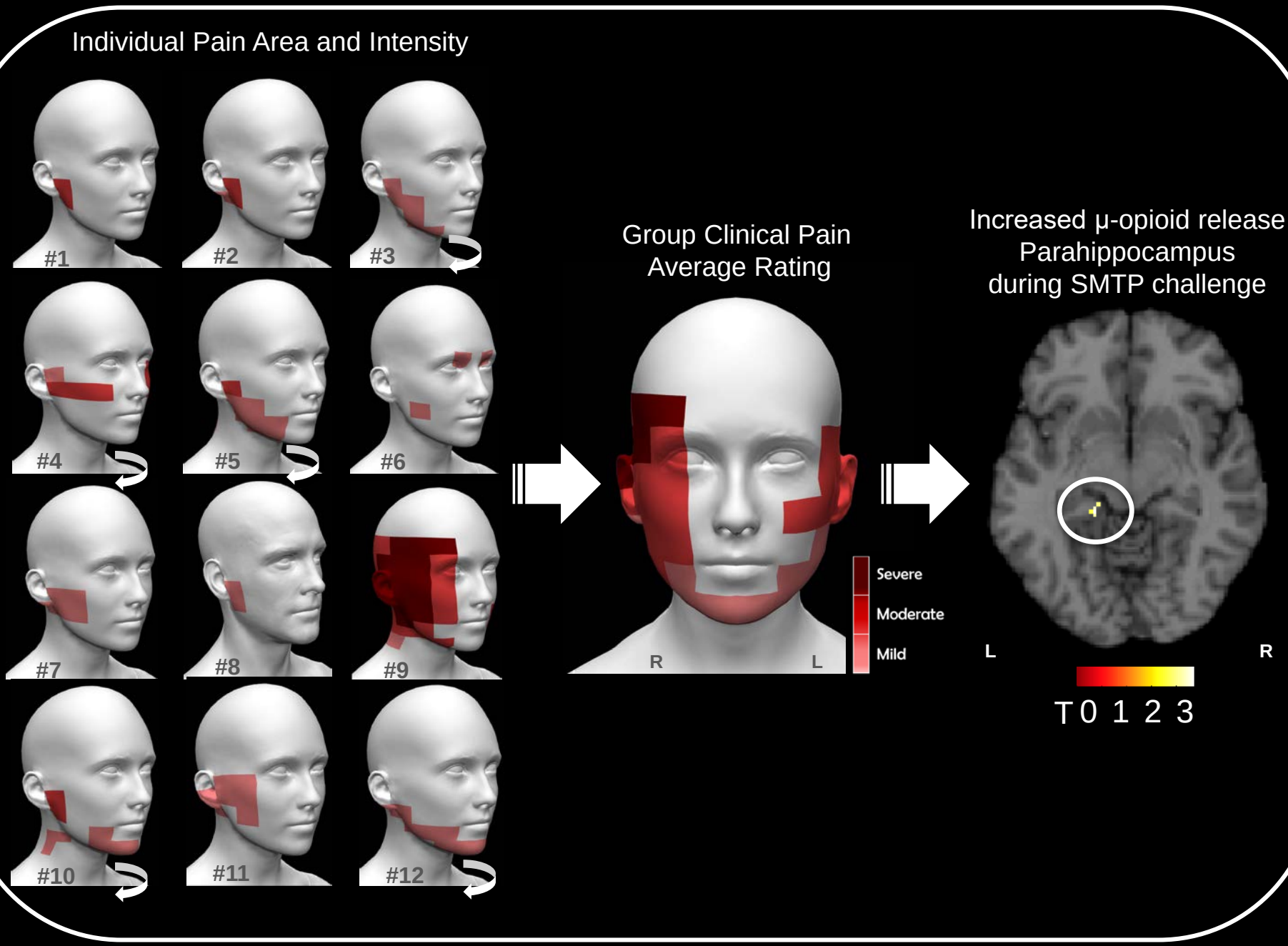
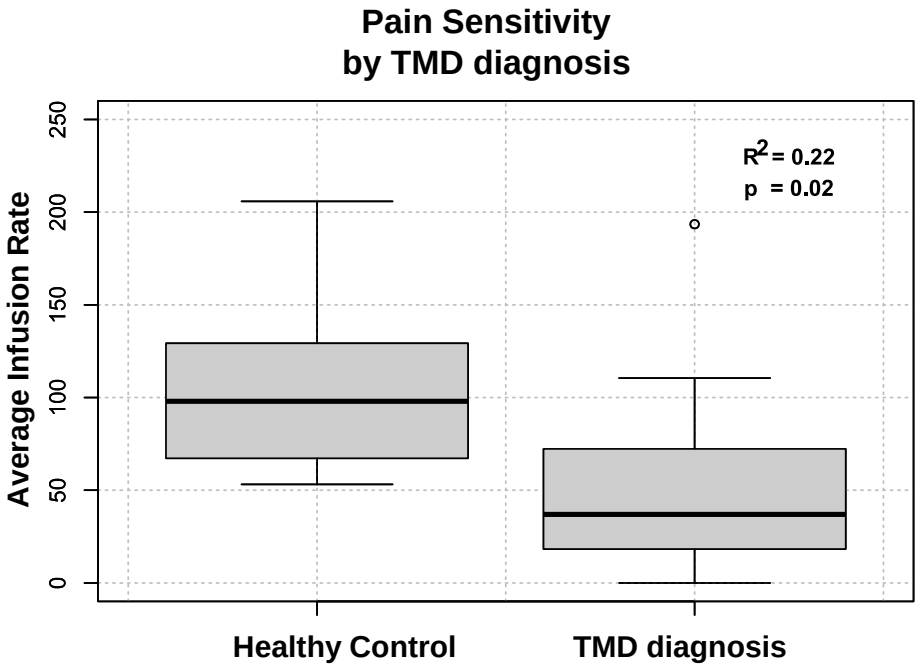
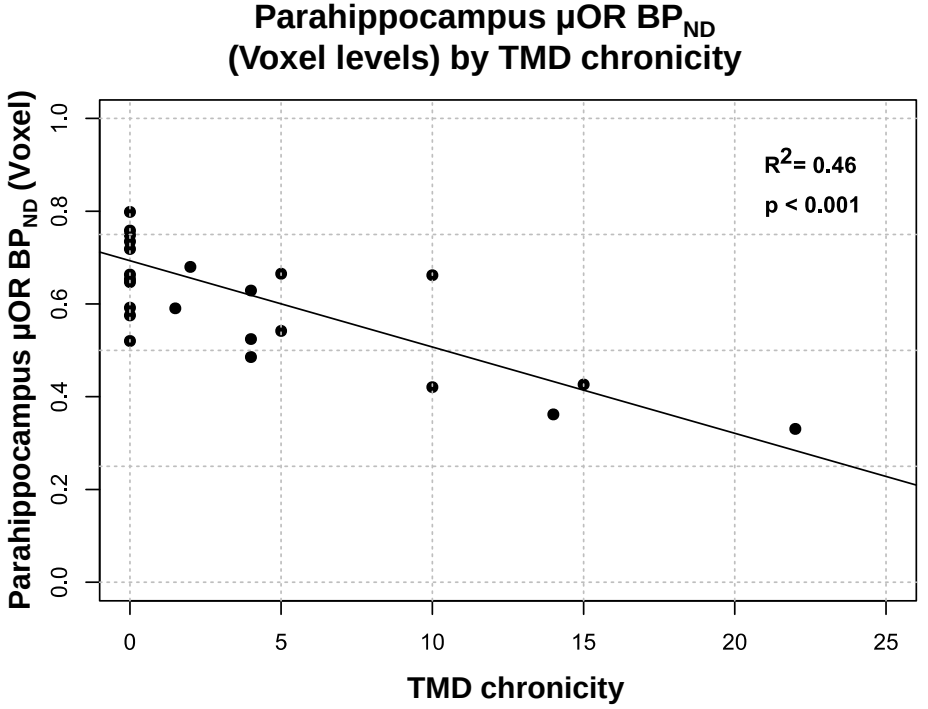


NIH-NIDCR U01 DE025633

Pain Sensitivity and the Endogenous μ-opioid System in TMD





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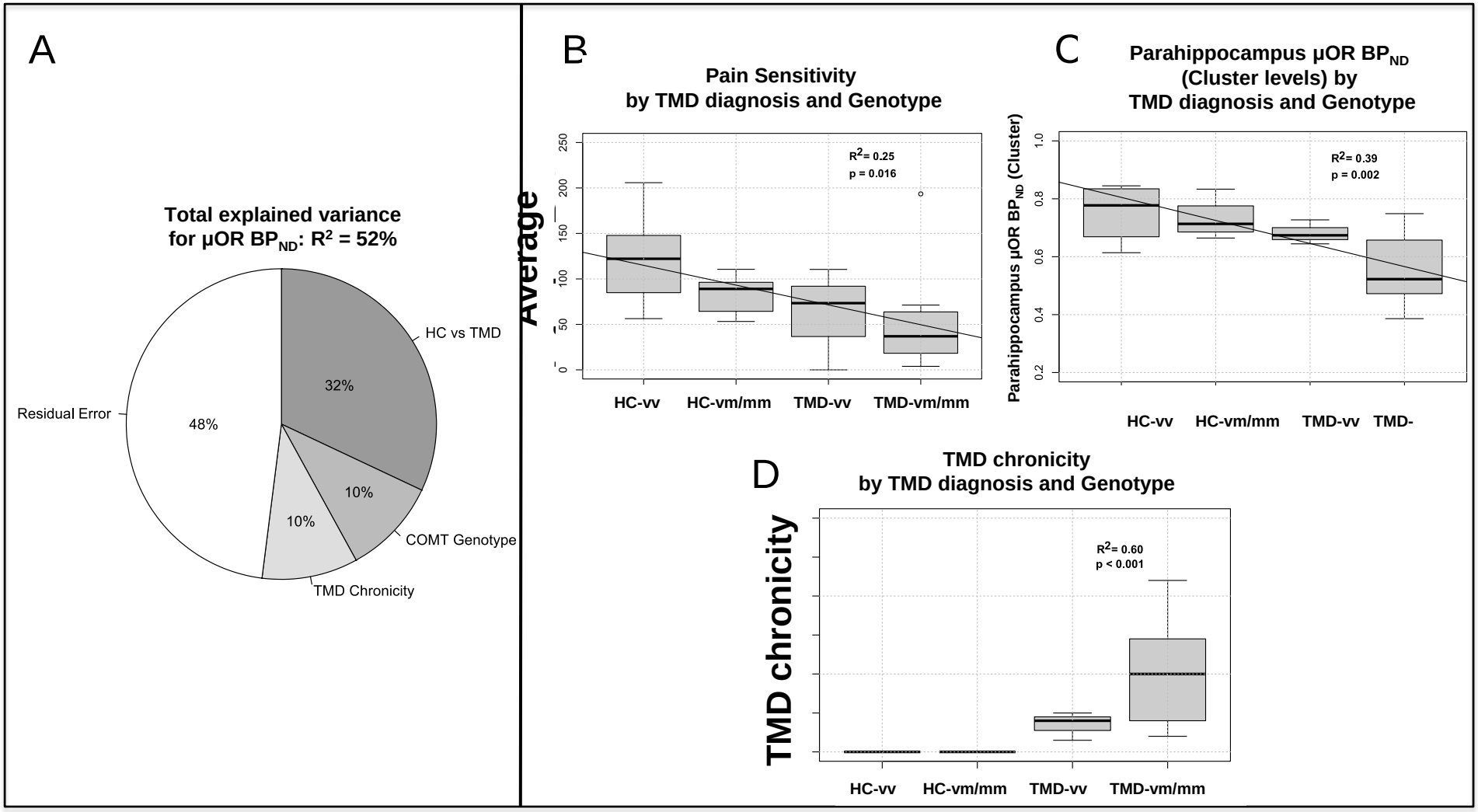
Mu-Opioid Activity And Genetics

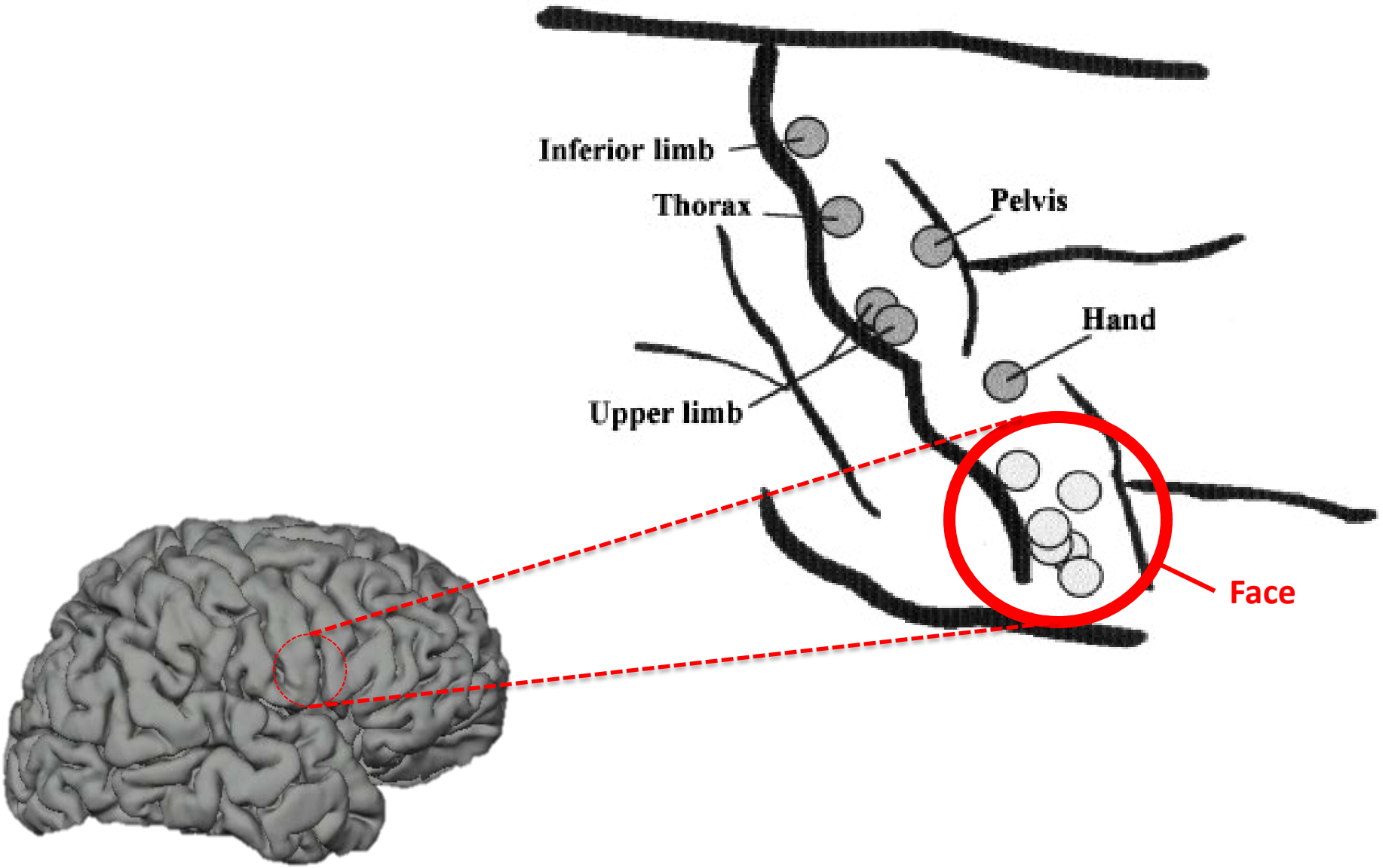
COMT Polymorphism Impact:
Chronic Pain Sensitivity and the μ-opioid Neurotransmission in the Limbic System



NIH-NIDCR U01 DE025633

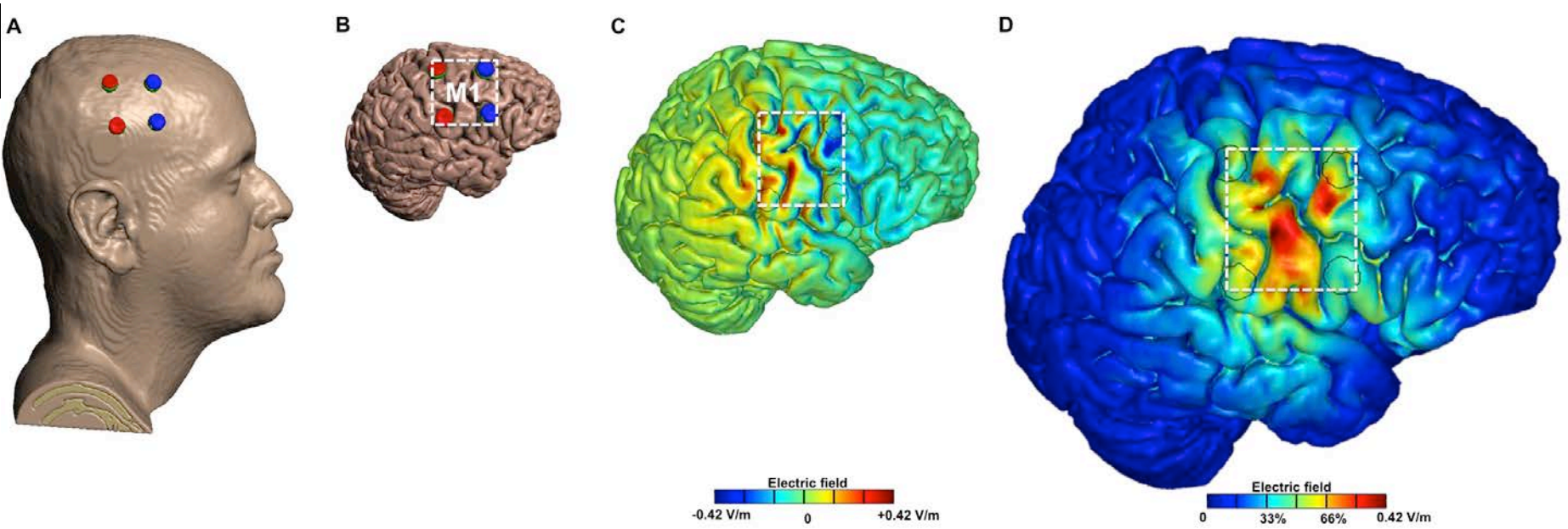
Precision in Pain Neuromodulation

INVASIVE Motor Cortex Stimulation In The Treatment Of Chronic Pain.



Nguyen et al, PAIN, Volume 82, Issue 3, 1999, 245 - 251

Non-Invasive H.O.P.E. lab M1 HD-tDCS Montage for Chronic Pain.



Donnell et al, 2015
H.O.P.E. Lab, University of Michigan

TMD: MONTH FOLLOW-UP

VAS 50% Responders from Week 1 to Week 6			
Group	Active	Sham	Total
<50% VAS decrease	3	8	11
≥50% VAS decrease	9	4	13
Total	12	12	24

Chi-Square $X^2=4.1958$ $p=0.04$

Donnell et al, 2015
H.O.P.E. Lab, University of Michigan

Location	Time Frame	Effect	Pain Sum	Ave Pain	Pain Area
Bilateral	Study	Week	0.0042	<0.0001	0.0027
		Group	0.0851	0.9845	0.1057
		Week*Group	0.3450	0.6252	0.3403
	Treatment	Day	0.0071	<0.0001	0.0052
		Group	0.1186	0.4078	0.0977
		PrePost	0.2945	0.0084	0.2237
		PrePost*Group	0.6300	0.1176	0.3567
Ipsilateral	Study	Week	0.0132	<0.0001	0.0095
		Group	0.1170	0.6522	0.1623
		Week*Group	0.3136	0.8908	0.2470
	Treatment	Day	0.1713	0.0013	0.0139
		Group	0.2058	0.6991	0.1932
		PrePost	0.2871	0.7001	0.4564
		PrePost*Group	0.2107	0.9903	0.3297
Contralateral	Study	Week	0.0083	<0.0001	0.0045
		Group	0.0735	0.9820	0.0758
		Week*Group	0.3852	0.0924	0.4903
	Treatment	Day	0.0005	<0.0001	0.0057
		Group	0.0747	0.4471	0.0553
		PrePost	0.0007	<0.0001	0.0035
		PrePost*Group	**0.0118**	**0.0012**	**0.0088**

*p-value is for Type 3 test of fixed effect from linear mixed model for particular time frame (over study or over treatment) of particular dependent variable.

Donnell et al, 2015
H.O.P.E. Lab, University of Michigan

Decrease in Pain Area and Intensity Only in the Side Contralateral to M1 Stimulation

Donnell et al, 2015
H.O.P.E. Lab, University of Michigan

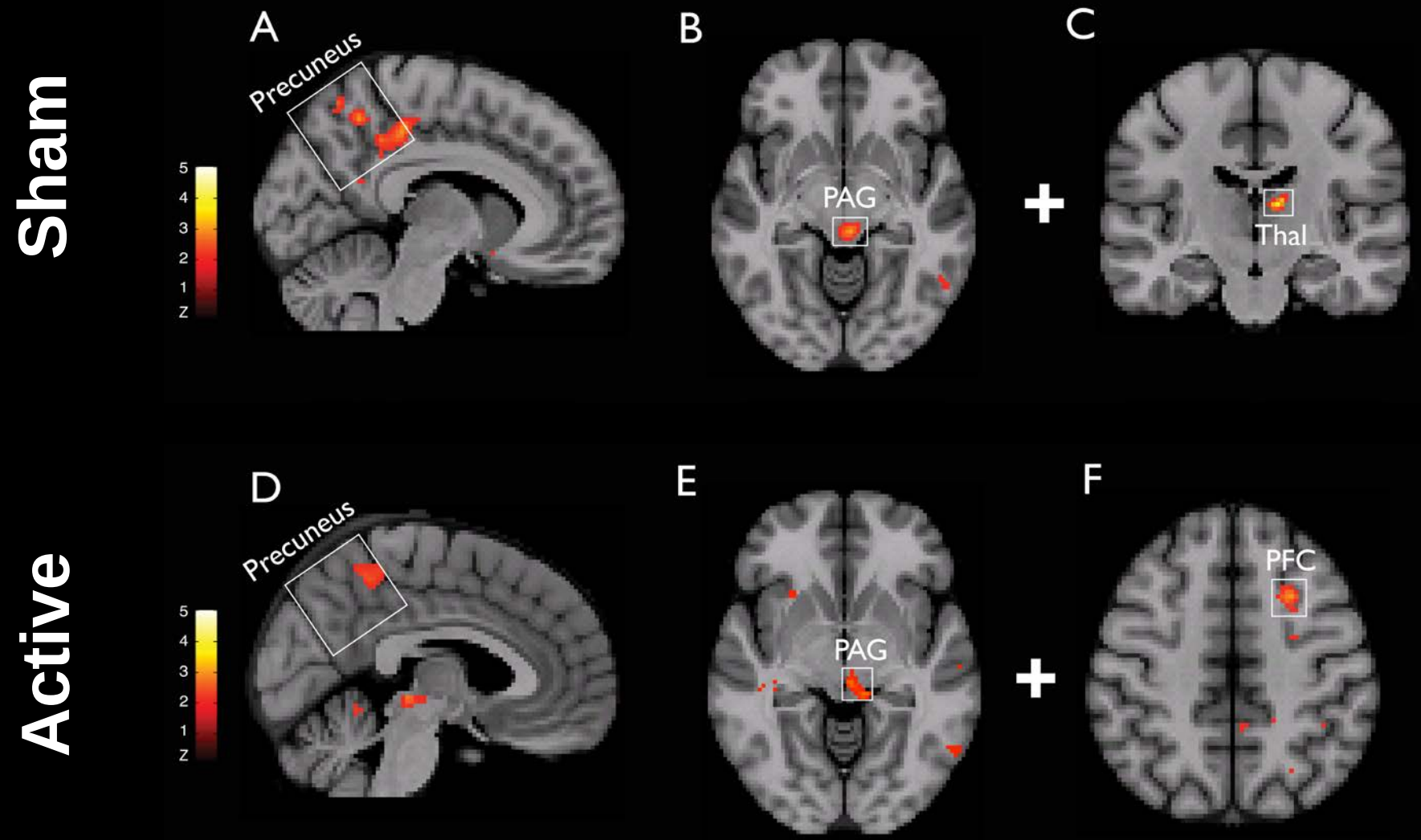
Mu-Opioid Activity And Neuromodulation

Neuromodulation

+

Molecular Neuroimage

μ-Opioid Activation During tDCS



DosSantos et al, 2014
H.O.P.E. Lab, University of Michigan

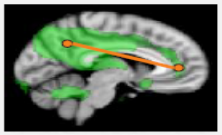
So what?

I can not read my patient's brain in the office!

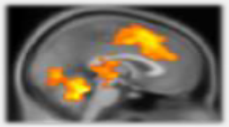
Imaging Data / Biomarkers

DTI
Tractography

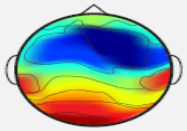
Gray Matter
Volumetry



Resting State
Analysis



Brain Activity



EEG

Non-Imaging Data Sources / Biomarkers

Passively Recorded Biometrics

Genotype

Wearables

Actively Reported Biometrics

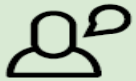
Experiential Sampling Program

Passively Recorded Psychometrics

Reaction Time

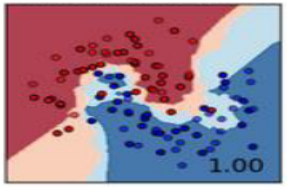
Voice Analysis

Actively Reported Psychometrics



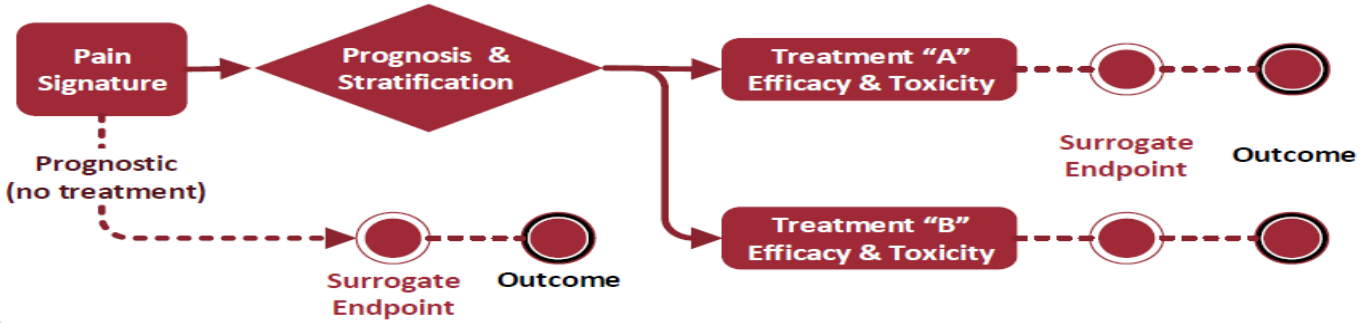
Item-Response Theory

Pain Signature



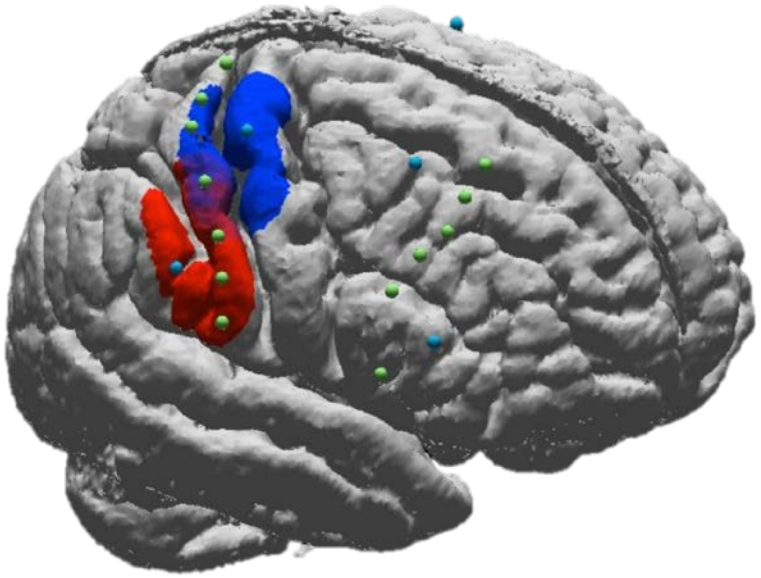
Clustering
Regression
Classification

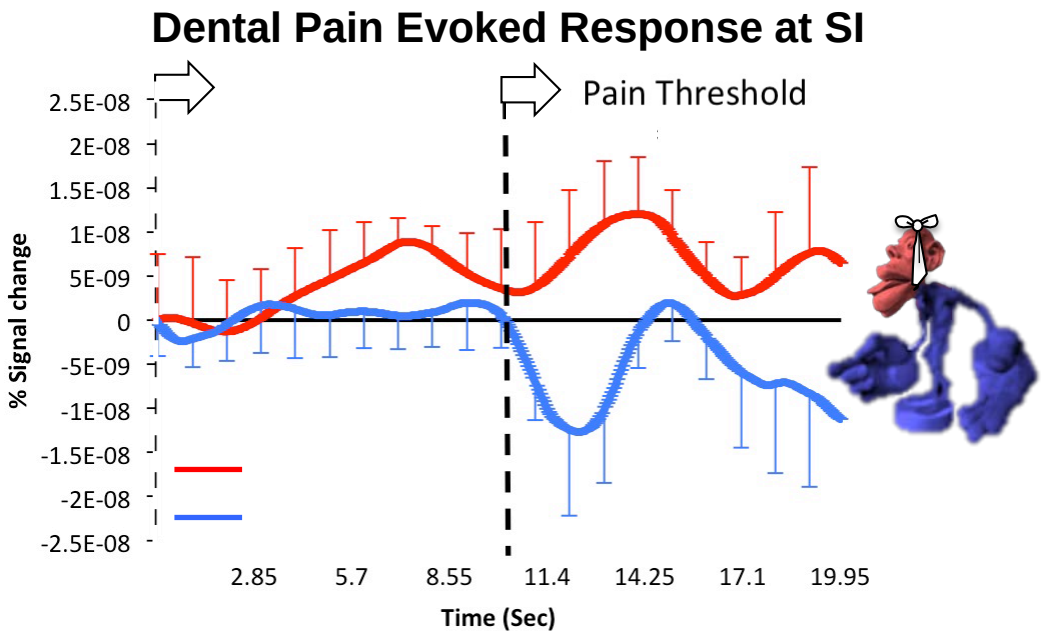
Clinical Applications



Slide kindly provided by
Dr. Sean Mackey, Stanford University

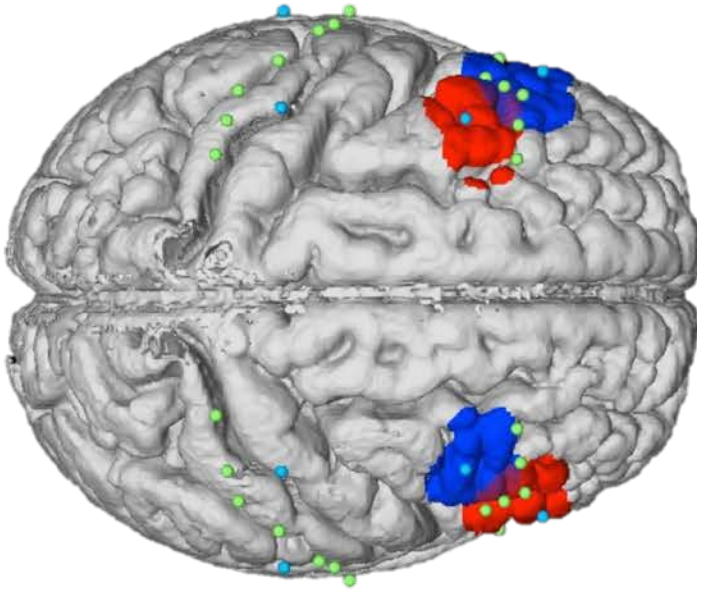
Michigan Clinical Augmented Reality Pain Unit (M-CARP)

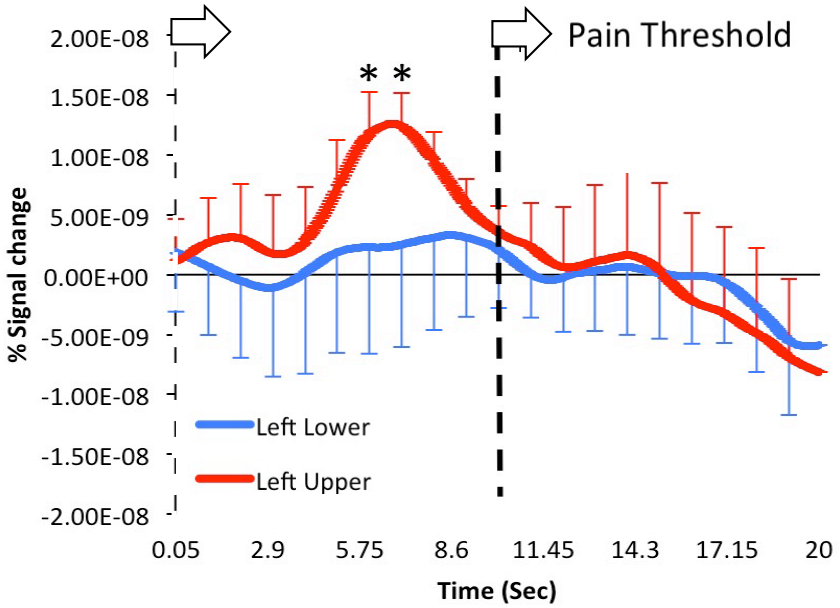


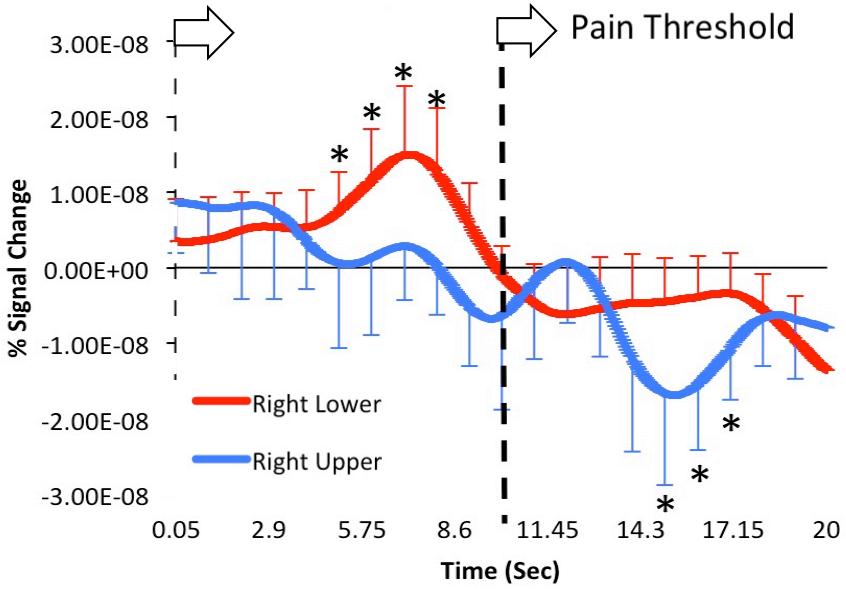


Colgate-Palmolive

Racek et al, 2015
H.O.P.E. Lab, University of Michigan

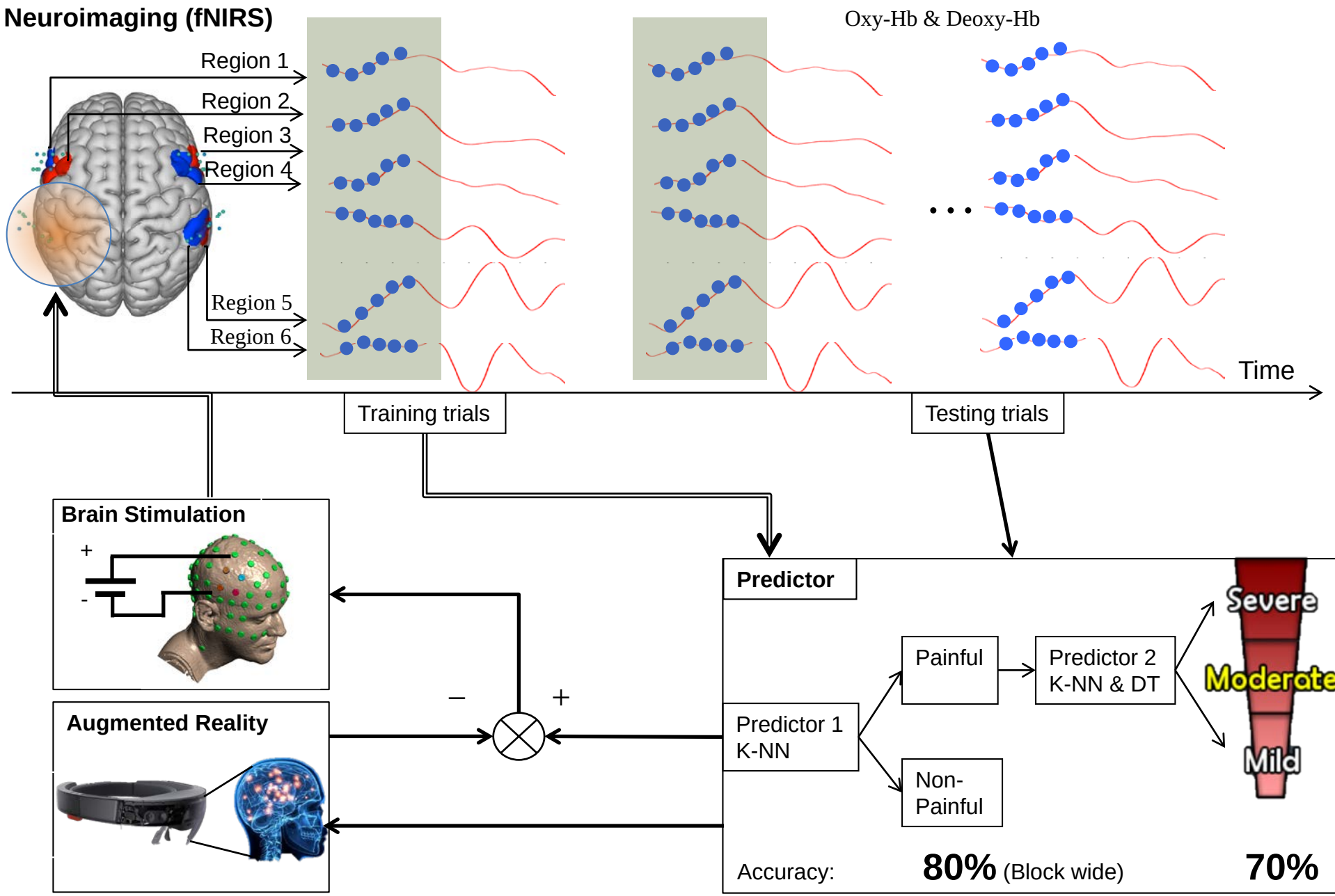






Racek et al, 2015
H.O.P.E. Lab, University of Michigan

Clinical Augmented Reality and Artificial Intelligence - CLARAi



K-NN: K Nearest Neighborhood DT: Decision Tree

CLARAi

Clinical Augmented Reality and Artificial Intelligence

CLARAi

Clinical
Augmented Reality

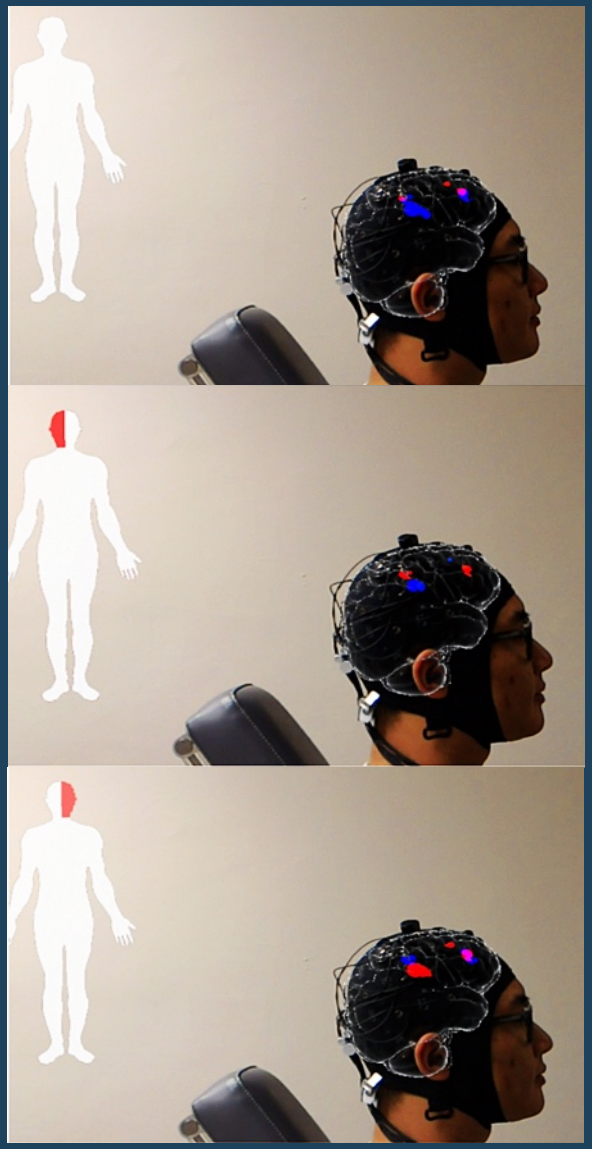
+

AI

Clinical
Artificial Intelligence

+

Real-Time
Neuroimaging



No Pain

Right Side Pain

Left Side Pain

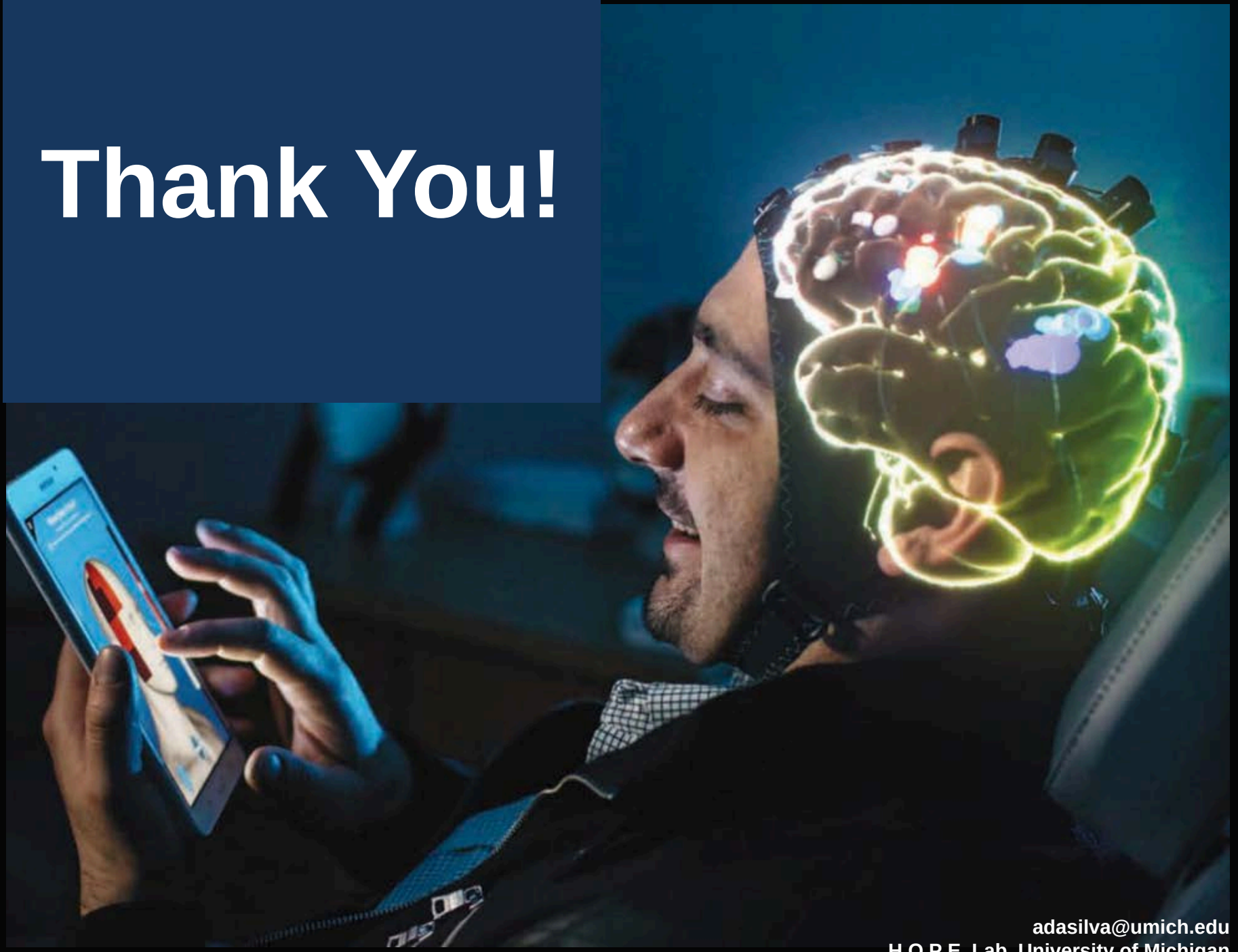
Hu et al, Under Review
H.O.P.E. Lab, University of Michigan

Hu et al, under review
H.O.P.E. Lab, University of Michigan

Conclusions

- Novel neuroscience-driven technologies have improved our ability to better detect and localize pain in the clinical environment
- The brain is presenting itself as an objective and reliable target for multiple emerging technologies to advance personalized treatment of chronic pain.

Thank You!



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