Developing Models For New Treatment Technologies  
Bringing Precision to the Pain Field

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Co-Director, fNIRS Laboratory, Center for Human Growth & Development (CHGD)  
Founder, Michigan Clinical Augmented Reality for Pain unit (M-CARP unit)  
Biologic & Materials Sciences Department, University of Michigan School of Dentistry
Disclosure: MoxyTech LLC (Co-Founder)
116 Million Americans With Chronic Pain

Costs $635 billion a year

Costs per patient additional $4.5-7.7 thousand in health care expenditures
<table>
<thead>
<tr>
<th></th>
<th>VAS</th>
<th>PainTrek Average</th>
<th>PainTrek Pain Area</th>
<th>PainTrek P.A.I.N.S.</th>
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</thead>
<tbody>
<tr>
<td>7:19pm. Tuesday (10/22/2013)</td>
<td>5.9</td>
<td>1.4</td>
<td>7.3%</td>
<td>3.5%</td>
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<tr>
<td>6:33pm. Monday (11/11/2013)</td>
<td>6.3</td>
<td>2.0</td>
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<td>3.6%</td>
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<td>6:07pm. Tuesday (10/22/2013)</td>
<td>5.7</td>
<td>2.1</td>
<td>36.4%</td>
<td>25.7%</td>
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</table>
EHR Collaboration

[Logos for Michigan, Pitt, and North Carolina universities, along with Internet2 and ICE]
What are the Targets in our Brains for Pain Relief?
3D-Immersive NeuroNavigation in Migraine

DaSilva et al, 2014
H.O.P.E. Lab, University of Michigan
Spontaneous Migraine Attacks
Mu-Opioid Activation during Allodynia

Migraine Allodynia

μ-Opioid Activation

Midbrain

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>AVE</th>
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<tbody>
<tr>
<td>Ictal</td>
<td>45.2</td>
<td>45.91</td>
<td>39.53</td>
<td>36.45</td>
<td>34.33</td>
<td>40.68</td>
<td>40.35</td>
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<tr>
<td>Interictal</td>
<td>49.44</td>
<td>48.78</td>
<td>48.87</td>
<td>40.62</td>
<td>46.87</td>
<td>47.78</td>
<td>47.06</td>
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DaSilva et al, 2014
Nascimento et al, 2014
H.O.P.E. Lab, University of Michigan

NIH-NINDS K23 NS062946
NIH-NINDS R01 NS094413
DANA Foundation’s Brain Award
Migraine Research Foundation
Chronic TMD
Mu-Opioid Activation during Masseteric Pain

Masseteric Pain Challenge

COMT Genotype
Increased μ-opioid

NIH-NIDCR R56 DE022637
NIH-NIDCR R01 DE025633
Under Review
H.O.P.E. Lab, University of Michigan
So what?

Can you do something to help me?
Neuromodulation
INVASIVE Motor Cortex Stimulation In The Treatment Of Chronic Pain.
Non-Invasive H.O.P.E. lab M1 HD-tDCS Montage for Chronic Pain.
## TMD: MONTH FOLLOW-UP

### VAS 50% Responders from Week 1 to Week 6

<table>
<thead>
<tr>
<th>Group</th>
<th>Active</th>
<th>Sham</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>&lt;50% VAS decrease</td>
<td>3</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>≥50% VAS decrease</td>
<td>9</td>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>12</td>
<td>24</td>
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</table>

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

Donnell et al, 2015
H.O.P.E. Lab, University of Michigan
<table>
<thead>
<tr>
<th>Location</th>
<th>Time Frame</th>
<th>Effect</th>
<th>Pain Sum</th>
<th>Ave Pain</th>
<th>Pain Area</th>
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<tbody>
<tr>
<td><strong>Bilateral</strong></td>
<td>Study</td>
<td>Week</td>
<td>0.0042</td>
<td>&lt;0.0001</td>
<td>0.0027</td>
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<tr>
<td></td>
<td></td>
<td>Group</td>
<td>0.0851</td>
<td>0.9845</td>
<td>0.1057</td>
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<tr>
<td></td>
<td></td>
<td>Week*Group</td>
<td>0.3450</td>
<td>0.6252</td>
<td>0.3403</td>
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<tr>
<td></td>
<td>Treatment</td>
<td>Day</td>
<td>0.0071</td>
<td>&lt;0.0001</td>
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<td></td>
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<td>Group</td>
<td>0.1186</td>
<td>0.4078</td>
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<tr>
<td></td>
<td></td>
<td>PrePost</td>
<td>0.2945</td>
<td>0.0084</td>
<td>0.2237</td>
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<tr>
<td></td>
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<td>PrePost*Group</td>
<td>0.6300</td>
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<tr>
<td><strong>Ipsilateral</strong></td>
<td>Study</td>
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<td></td>
<td>Group</td>
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<td>Week*Group</td>
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<td>Treatment</td>
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<td>0.1713</td>
<td>0.0013</td>
<td>0.0139</td>
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<tr>
<td></td>
<td></td>
<td>Group</td>
<td>0.2058</td>
<td>0.6991</td>
<td>0.1932</td>
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<td></td>
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<td>PrePost</td>
<td>0.2871</td>
<td>0.7001</td>
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<td>PrePost*Group</td>
<td>0.2107</td>
<td>0.9903</td>
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<tr>
<td><strong>Contralateral</strong></td>
<td>Study</td>
<td>Week</td>
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<td>Group</td>
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<td>Week*Group</td>
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<td>PrePost*Group</td>
<td>0.0118</td>
<td>0.0012</td>
<td>0.0088</td>
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</tbody>
</table>

*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.
There were no significant differences between sham and active tDCS group.
μ-Opioid Activation During tDCS
μ-Opioid Activation During tDCS

DosSantos et al, 2014
H.O.P.E. Lab, University of Michigan
μ-Opioid Activation During tDCS

DosSantos et al, 2014
H.O.P.E. Lab, University of Michigan
What is the Chronic Effect of Sham and Active Neuromodulation?
Thalamus ACC Anterior Insula
GABA (AIU) 
Glutamate

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

MICHR Clinical Trial Planning
CTSA High-Tech funding: UL1RR024986
Pre-Treatment Glx within the Anterior Cingulate Predicts Subsequent Clinical Response to Sham and Active tDCS

Sham tDCS
- $r = -0.81$
- $p < 0.001$

Active tDCS
- $r = -0.87$
- $p < 0.001$

Foerster et al, 2015
H.O.P.E. Lab, University of Michigan
So what?

I can not read my patient’s brain in the office!
So what?
Dental Pain Evoked Response at SI

Racek et al, 2015
H.O.P.E. Lab, University of Michigan
Dental Pain Evoked Response at Left Prefrontal Cortex

Dental Pain Evoked Response at Right Prefrontal Cortex

Racek et al, 2015
H.O.P.E. Lab, University of Michigan
**HIGHER CLINICAL PAIN**

1. **Stronger PFC-S1 Functional Connectivity**

2. **Stronger Activity in PFC During Pain Expectation**

3. **Faster and Stronger Cold-Related Activity in S1**

4. **Stronger Pain-Related Activity in S1**

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**Functional Connectivity**

**Functional Correlation**

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*Hu et al*

Under Review

H.O.P.E. Lab, University of Michigan
Pattern Recognition + Clinical Augmented Reality

Neuroimaging (fNIRS)

Region 1
Region 2
Region 3
Region 4
Region 5
Region 6

Oxy-Hb & Deoxy-Hb

Training trials
Testing trials

Brain Stimulation

Augmented Reality

Predictor

Painful
Non-Painful

Predictor 1
K-NN

Predictor 2
K-NN & DT

Accuracy: 80% (Block wide)

K-NN: K Nearest Neighborhood DT: Decision Tree