The Intersection of Physics, Opiates and Recovery

Newport Brain Research Laboratory
Brain Treatment Center
NAADAC 2016, Minneapolis
Newport Brain Research Laboratory/Brain Treatment Center

Mission Statement

Newport Brain Research Laboratory (NBRL) is a life science company focused on technology in brain science. NBRL has the capability to uniquely image the brain, identify areas of the brain that are not functioning properly and, most importantly, restore the problematic regions of the brain to optimal neurological function using non-invasive neuromodulation.
Strategic Partnerships

Keck Medical Center of USC
Center for Neurorestoration

SWEDISH NEUROSCIENCE INSTITUTE

UC San Diego School of Medicine

St. Joseph Hoag Health
Hoag • Mission • St. Joseph • St. Jude
In alliance with CHOC Children's

UNIFORMED SERVICES UNIVERSITY
of the Health Sciences

RANCHO Research Institute

Rancho Los Amigos National Rehabilitation
Scope of the Problem

- TBI called the “signature injury” of OEF/OIF
- 33% of all patients and 60% of patients with blast related injuries seen at Walter Reed had TBI (Okie, 2005)
  - Veterans Health Initiative Traumatic Brain Injury
- 13.8% of Gulf War Vets suffer from PTSD
  - 50% do not seek treatment, of the half that do only 25% get “minimally adequate” treatment
  - Rand, Center for Military Health Policy Research
- 22 suicides/day among US Military Veterans, more active duty personnel die by their own hand than combat in 2012
  - Department of Veterans Affairs, Mental Health Services
DoD releases 2nd quarter suicide figures

By Patricia Knee, Staff writer 9:54 a.m. EDT October 1, 2015

Suicides among active-duty service members rose by 20 percent in the second quarter of this year to 71, according to a new report released Wednesday by the Defense Department.

The Marine Corps had the highest percentage increase, 12 suicides, up from three the previous quarter.

The Army had 26 active-duty suicides, the Air Force, 17, and the Navy, 14, according to...
VA Polytrauma Model
Chronic Pain and Opioids

More physician prescribed opioid fatalities than illicit cocaine and heroin combined
Pain and Opioids

Mortality = “Tip of the iceberg”

Source: CDC - Injury Prevention & Control – Prescription Pain Killer Overdoses
http://www.cdc.gov/homeandrecreationalssafety/rxbrief/
Chronic Pain and Brain Function
NIH Funded Study

• An NIH sponsored study utilizing f-MRI and diffusion tensor imaging (DTI) identified areas of the brain that may predispose individuals to chronic pain. The results, published in the journal *Pain*, support the growing idea that the brain plays a critical role in chronic pain.

• “We may have found an anatomical marker for chronic pain in the brain...Our results suggest that the structure of a person’s brain may predispose one to chronic pain. We were surprised how robust the results were and amazed at how well the brain scans predicted persistence of low back pain,”

  • Vania Apkarian, Ph.D., senior author of the study and professor of physiology at Northwestern University Feinberg School of Medicine


Functional MRI (f-MRI) and Addiction

- Morphologic changes of the addicted brain are observable

f-MRI The brains response to cocaine. Arrows point to the anterior cingulate area, which is activated in cocaine addicted patients (left), but not in healthy volunteers (right). (Wexler, et al. 2001)
Functional Interaction between Medial Thalamus and Rostral Anterior Cingulate Cortex in the Suppression of Pain Affect

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Abstract

The medial thalamic parafascicular nucleus (PT) and the rostral anterior cingulate cortex (ACC) are implicated in the processing and suppression of the affective dimension of pain. The present study evaluated the functional interactions between PT and ACC in mediating the suppression of pain affect in rats following administration of morphine or carbachol (acetylcholine agonist) into PT. Vocalizations that occur following a brief noxious tail shock (vocalization after discharges) are a validated model of pain affect, and were preferentially suppressed by injection of morphine or carbachol into PT. Vocalizations that occur during tail shock were suppressed to a lesser degree, whereas, spinal motor reflexes (tail flick and hindlimb movements) were only slightly suppressed by injection of carbachol into PT and unaffected by injection of morphine into PT. Blocking glutamate receptors in ACC (NMDA and non-NMDA) by injecting 2-amino-5-phosphonovaleric acid (AP-5) or 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX) produced dose-dependent antagonism of morphine-induced decreases in vocalization thresholds. Carbachol-induced increases in vocalization thresholds were not affected by injection of either glutamate receptor antagonist into ACC. The results demonstrate that glutamate receptors in the ACC contribute to the suppression of pain affect produced by injection of morphine into PT, but not to the suppression of pain affect elicited by intrathecal injection of carbachol.
Neuromodulation

• Neuromodulation – Refers to an emerging class of medical therapies that target the nervous system for restoration of function, relief of pain, and/or to control symptoms of depression/anxiety.

• Invasive Neuromodulation

• Non-Invasive Neuromodulation
Neuromodulation (Invasive)

• Deep Brain Stimulation Video (Before and After)
Neuromodulation (Invasive)

- Surgical (Invasive) Neuromodulation, called Deep Brain Stimulation (DBS), has been a rapidly evolving area of neurosurgical intervention and is now considered “standard of care” for drug resistant Parkinson’s and OCD.
Neuromodulation (Non-Invasive)

• Despite good outcomes with DBS, patients have been largely unwilling to undergo brain surgery with craniotomies.
  • Less than 30% of candidates eligible for DBS surgery agree to have it performed.

• Race to develop a “non-invasive” neuromodulation modality!
  • Repetitive Transcranial Magnetic Stimulation (rTMS)
    • Magnetic energy directed to the left dorsolateral prefrontal cortex (10 Hertz at 120%)
    • FDA approved for treatment of depression in 2008, now widely available.
  
• Magnetic e-Resonance Therapy (MeRT) technology
  • Customized application of rTMS treatment: Guided by brain map (q-EEG), personalized, precision, prime frequency (.00 Hertz) at 60-80% of threshold.
  • Early Data: Almost twice as effective as rTMS in head-to-head clinical trials.
  • Much broader application than just depression: Autism Spectrum Disorder (ASD), PTSD, Depression/Anxiety, and Addiction/Substance Use Disorder.
Neuromodulation (Non-Invasive)

Non-pharmaceutical (no systemic side effects), non-invasive (painless), similar exposure to a standard MRI (almost no adverse events), with strong clinical efficacy
CEPAC, a regional body, whose goal is to provide objective, independent guidance on the application of medical evidence to clinical practice and payer policy decisions across New England.

December, 2011: CEPAC reviewed the AHRQ evidence on rTMS and voted that the evidence was adequate to demonstrate that rTMS was as good as, or better than existing care for patients with treatment-resistant depression (drugs + psychotherapy).

CEPAC = Comparative Effectiveness Public Advisory Council
AHRQ = Agency for Healthcare Research and Quality
Neuromodulation (Non-Invasive) Safety Profile

Table 1: Potential side effects of TMS. Consensus has been reached for this table.

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Single-pulse TMS</th>
<th>Paired-pulse TMS</th>
<th>Low frequency TMS</th>
<th>High frequency TMS</th>
<th>Theta burst</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure induction</td>
<td>Rare</td>
<td>Not reported</td>
<td>Rare (usually protective effect)</td>
<td>Possible (1.4% crude risk estimate in epileptic patients; less than 1% in normals)</td>
<td>Possible (one seizure in a normal subject during TBS) (see para 3.3)</td>
</tr>
<tr>
<td>Transient acute hypomnasia induction</td>
<td></td>
<td>No</td>
<td>Rare</td>
<td>Possible following left prefrontal stimulation</td>
<td>Not reported</td>
</tr>
<tr>
<td>Transient headache, local pain, neck pain, toothache, paraesthesia</td>
<td>Possible</td>
<td>Likely possible, but not reported/ addressed</td>
<td>Frequent (see para. 3.3)</td>
<td>Frequent (see para. 3.3)</td>
<td>Possible</td>
</tr>
<tr>
<td>Transient hearing changes</td>
<td>Possible</td>
<td>Likely possible, but not reported</td>
<td>Possible</td>
<td>Possible</td>
<td>Not reported</td>
</tr>
<tr>
<td>Transient cognitive/neuropsychological changes</td>
<td>Not reported</td>
<td>No</td>
<td>Overall negligible (see Section 4.6)</td>
<td>Overall negligible (see Section 4.6)</td>
<td>Transient impairment of working memory</td>
</tr>
<tr>
<td>Burns from scalp electrodes</td>
<td>No</td>
<td>No</td>
<td>Not reported</td>
<td>Occasionally reported</td>
<td>Not reported, but likely possible</td>
</tr>
<tr>
<td>Induced currents in electrical circuits</td>
<td>Theoretically possible, but described malfunction only if TMS is delivered in close proximity with the electric device (poo-makers, brain stimulators, pumps, intracardiac lines, cochlear implants)</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Structural brain changes</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Inconsistent</td>
<td>Inconsistent</td>
<td>Not reported</td>
</tr>
<tr>
<td>Histocompatibility</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Inconsistent</td>
<td>Inconsistent</td>
<td>Not reported</td>
</tr>
<tr>
<td>Other biological transient effects</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
Neuromodulation (Non-Invasive) Safety Profile

“In summary, based on *ex vivo* and *in vivo* studies, it appears that TMS can be safely applied to patients...it is worth noting that exposure to electromagnetic fields appears safe at levels even greater than those possible with TMS (Gandhi, 2002; Martens, 2007)”
Neuromodulation (Non-Invasive) Adverse Effects

- Temporary discomfort/pain at scalp
- Temporary headache
- Overstimulation (excitation)
- Seizure (estimate 1:100,000 – 1:500,000)

(Note: Nintendo warns of 1:4000 seizure possibility)
Quantitative EEG (q-EEG)

q-EEG is painless and takes only 20-30 minutes
Quantitative EEG - Concepts

- Measures six brainwave clinical bands

- Every individual has a “cognitive fingerprint” with an intrinsic wavelength profile...deficits can be picked up when an area of the brain deviates from the intrinsic wave signature

Major depression manifests as abnormality of the left dorsolateral prefrontal cortex (DLPFC).
Repetitive Transcranial Magnetic Stimulation (rTMS)

- FDA approved treatment for drug-resistant major depression (2008)
  - 1st Generation – Transcranial Magnetic Stimulation (TMS)
    - Alpha wave fixed at 10.0 Hz via single coil device delivered to the LDLPFC = 33% response rate for drug-resistant depression
Magnetic e-Resonance Therapy (MeRT)

- **2nd Generation – Magnetic e-Resonance Therapy (MeRT)**
  - MeRT (deep signal) across multiple bands, personalized to an individuals intrinsic profile, and guided by q-EEG to specifically targeted areas (brain navigation)
PTSD – Prospective, Double Blind, Placebo-Controlled, Randomized Controlled Trial

• 86 subjects (77 M & 8 F) / Average Age 37.8 yrs / Moderate-Severe PTSD

• Phase 1: patients randomly assigned into one of two treatment groups - Active MeRT Treatment or SHAM (Placebo Control) Treatment - for two weeks. Technicians delivering treatment were blinded.

• Severity of clinical symptoms was evaluated using quantitative rating scale - PTSD Checklist Military (PCL-M) - by a research clinician who was blinded to the treatment condition.
  • PCL-M: a well-recognized and validated questionnaire scoring range 0-80
  • Symptoms at baseline varied from ‘moderate’ to ‘severe’ (38-80)

• Phase 2: two-week, Open-Label Trial during which all received active MeRT treatment.
Clinical Improvement in PCL-M following MeRT and Sham

Phase 1 Double Blind: Repeated Measure ANOVA $F_{1,49} = 4.65$, $p = 0.03$
Phase 2 Open Label: Single Variable ANOVA $F_{1,50} = 0.04$, $p = 0.85$
Neuromodulation (Non-Invasive) MeRT Studies - PTSD

- Average 63% reduction in symptom severity (Fig.1; p<0.0001).
- Accordingly, patients demonstrated EEG improvement in alpha power, coherence, and reduction in slow waves.

*Figure 1. PCL-M change after MRT*
Neuromodulation (Non-Invasive) MeRT Studies – TBI/PTSD

- Corroboration of PCL-M scores (subjective questionnaire) with q-EEG brain imaging (objective study)
A Case . . .

Note: Jeff has provided consent to share his case
Before Treatment . . .

- **Insomnia** -“I haven’t had a good night of sleep in 11 years”
  - Medicates & drinks himself to sleep
- **Chronic Pain**
  - Failed back surgery x 2
  - 170 morphine equivalents daily
  - 20 pills/day (antidepressants, muscle relaxants, pain pills, etc)
  - “Every antidepressant known to man . . .”
- Utilized every available VA treatment modality for PTSD and addiction.
- Anger issues, road rage, hypervigilance in crowds, depressed mood, etc.
After 6 weeks of MeRT treatment:
• Restful sleep
• Anger dissipated
• Upbeat mood
• Chronic pain dramatically reduced (hyperalgesia resolved)
  • Off all prescription drugs
  • Takes 1 pill/day (Vitamin D)
• Completed a Masters of Social Works (Addiction Counseling)
• Applying for PhD programs
SGT Warren and SGT Stephenson provided consent to share their stories.
MeRT Trial 002 - PTSD

Findings from PTSD study...

- 63% reduction in symptom severity (PCL-M).
- 96% reported improved quality of sleep.
- VAS Pain Scores reduced from 7.4 to 2.7.
- **25% voluntarily weaned off opioids**
- 86% of Veterans voluntarily decreased opioid use.
- 77% of Veterans voluntarily decreased alcohol use.

*Data points still holding at 1-year marker . . .
Quantitative EEG

Pre Treatment

Post Treatment
“All truth passes through three stages. First, it is ridiculed. Second, it is violently opposed. Third, it is accepted as being self-evident”

--

Arthur Schopenhauer, German Philosopher (1788-1860)
So . . . Where are we with all of this?
Department of Defense

• Tinker Airforce Base . . .
  Randomized, Double-Blind, Placebo-Controlled Trial Underway

• US Special Operations Command . . .
  Two-Site Trial (CA and FL) being mounted by Uniformed Services for Health Sciences (USUHS)

“The USSOCOM Command Surgeon and several senior members of the Special Operations Community have witnessed some remarkable anecdotal results from the treatment provided by NBRL; some of which defy traditional medical explanation. We are excited about the opportunity to further explore this method of treatment to help our active duty and veteran teammates in DOD.”

CAPT (SEAL) J Doolittle, USN, Director, Preservation of the Force and Family (POTFF)
New research areas. — As indicated in the House report, the conferees encourage VA to create a Center of Innovation for research support and use as candidates for initial research hyperbaric oxygen therapy and Magnetic EEG/EKG-guided Resonance Therapy.
A BILL
To direct the Secretary of Veterans Affairs to carry out a pilot program to provide access to magnetic EEG/EKG-guided resonance therapy technology to veterans.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.
This Act may be cited as the “No Hero Left Untreated Act”.

SEC. 2. FINDINGS.
Congress finds the following:
(1) Magnetic EEG/EKG-guided Resonance Therapy technology (in this section referred to as “MeRT technology”) has successfully treated more than 400 veterans with post-traumatic stress disorder, traumatic brain injury, military sexual trauma, chronic pain, and opiate addiction . . . .

9/21 - PASSED THROUGH FULL COMMITTEE MARK-UP AND REPORTED FAVORABLY TO THE HOUSE.
Based on Veteran results, a pilot was conducted through workers compensation to assess efficacy for injured workers with chronic pain and opioid dependence:

- All subjects reduced opioid dose by 50% within the first month.
- Sixty-six percent (66%) successfully weaned off opioids.
- The remaining third (33%) were able to reduce to a safer, low dose, opioid regimen.
- One case went from 700 morphine equivalents daily (MED) to 80 MED’s. This patient felt well enough to find a new job and return to work after 18 years of “total disability” and unemployment.
- Subjects reported “very limited” or “no withdrawals” . . . the weaning process characterized as a “soft landing.”
Private Insurance Pilot Data
Neuropsych Testing
MeRT Summary

• MeRT is an innovative medical technology demonstrating strong clinical efficacy for opioid dependence.
  • Clinical efficacy is corroborated by post-treatment brain imaging.

• MeRT has an excellent safety profile.
  • Non-invasive, minimal side effects or adverse events, in an outpatient setting with the same exposure/energy of an MRI.

• MeRT is cost effective.
  • A fraction of the cost of lifetime opioid treatment

• MeRT transforms Quality of Life factors.
  • Impossible to quantify the impact for patients and their families. Patients (and their family members) identify transformative quality of life changes
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