Direct Brain Interfaces for Memory Restoration

Dan Rizzuto, PhD
Nia Therapeutics
Deep Brain Stimulation Treats a Variety of Disorders

• Approved for Parkinson’s disease for 20 years
• Now being used to treat Tourette’s Syndrome & OCD
• Major depression is under investigation
Restoring Active Memory (RAM) is a DARPA project to develop brain stimulation therapies to treat memory impairment due to TBI.
“Traumatic brain injury (TBI) is an alteration in brain function, or other evidence of brain pathology, caused by an external force.”

Impairments in memory, attention, and learning are the hallmark symptoms of TBI.
TBI is also common in the elderly due to falls.

In Japan, motor vehicle collisions are the #1 cause of TBI.
50-60 MILLION
New TBI cases occur each year, *worldwide*

3.2 MILLION
Americans are disabled due to TBI

379 THOUSAND
U.S. military service members have a TBI
Patients with TBI Have Limited Options

Cognitive Rehabilitation Therapy (CRT) is the only treatment for TBI

There is limited evidence that CRT is effective
The RAM Team
Direct Brain Recording & Stimulation

- Studies performed in patients with epilepsy
- Patients temporarily implanted with 100+ electrodes for ~2 weeks
- We perform memory testing, collect ECoG recordings & administer stimulation daily
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Big Data Drives Therapy Development

Over the past 3.5 years, we have:

- Tested 300+ subjects
- Administered 1,500+ memory sessions
- Recorded from 20k+ electrodes

memory.psych.upenn.edu/RAM_Public_Data
We Use Free Recall to Measure Memory

- The most sensitive measure of human memory
- Commonly used to diagnose memory impairment
Good memory is associated with an increase in high-frequency activity in distributed brain regions.
For each patient, words sorted into *Recalled* and *Forgotten* classes

Spectral power extracted from all ECoG electrodes during the *Encoding* period

Logistic regression is used to learn the spectral features that predict recall
Machine Learning Predicts Memory Performance from Brain Biomarkers

Ezzyat et al. (2017) Current Biology
Brain Stimulation Changes Memory Performance

- Each session has stim and no-stim lists
- Randomized, controlled, blinded design
- The state of the brain matters!
- Stim improves memory when memory is poor
- Stim impairs memory when memory is good

Ezzyat et al. (2017) *Current Biology*
Closed-loop Stim Reliably Improves Memory

- Machine learning used to estimate each patient’s brain state in real-time
- Stimulation delivered only during poor memory states
- 15% improvement with stimulation of lateral temporal cortex (LTC)

Ezzyat et al. (2017) Current Biology
Evidence of Effectiveness in TBI

- Some subjects in our study had a history of TBI
- Subjects with TBI show a numerically greater performance boost with stimulation

Unpublished data

<table>
<thead>
<tr>
<th></th>
<th>% Change in Recall</th>
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<tbody>
<tr>
<td>Non-TBI</td>
<td>N=8</td>
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<tr>
<td>TBI</td>
<td>N=3</td>
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0  10  20  30  40
% Change in Recall
The RAM Technology in Action
Stimulating Temporal Cortex is Most Effective

Kucewicz et al. (2018) Brain
The RAM System Concept
The RAM System Concept

Four depth electrodes:
- 64 channels of sensing
- 4 channels of stim

Cranial implant

Earpiece w/battery
The RAM System Concept

Clinician interface

Cloud-based machine learning algorithms
The Future of Cognitive Enhancement
Executive Function

Emotional Control

Attention

Memory
Future Directions

- Multi-target stimulation
- Stimulation during retrieval
- Chronic stimulation
- Improved machine learning algorithms
- Low-power sensing and stimulation ASICs
Electrical Stimulation Reinstates the Biomarkers of High Performance

• Stimulation produces changes in oscillatory power across the brain
• When delivered during the poor memory states, it moves the brain into a good memory state

Ezzyat et al. (2017) Current Biology