Targeted Neuroplasticity Training (TNT)

Or... How do we get our military personelle to take speed so they can get sick of winning!

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8 April 2016

TNT DARPA Team

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Cognitive-skill training is vital part of fulfilling national security mission

TNT Goal: Faster, more effective cognitive training for a variety of DoD applications

DoD applications of interest to the TNT program include, but are not limited to:

© Armin Weigel

Tactical Operations Center (TOC)

© Staff Sgt Justin Weaver

Foreign Language

© US Navy

Cryptography

© US Army

Intelligence

TNT – enhancing cognitive skill learning

Vision: enhancing cognitive skill learning in healthy adults by using noninvasive peripheral neurostimulation to promote synaptic plasticity in the brain

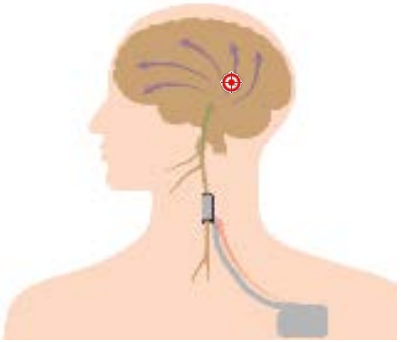
Cognitive Training Protocols

© US Army

Engage task-specific brain regions

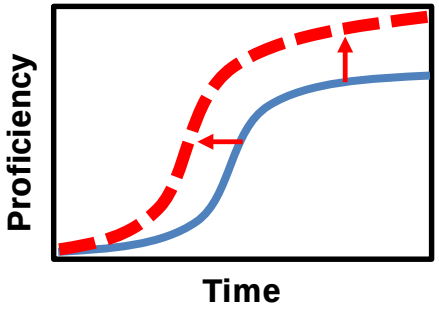
+

Peripheral Nerve Stimulation



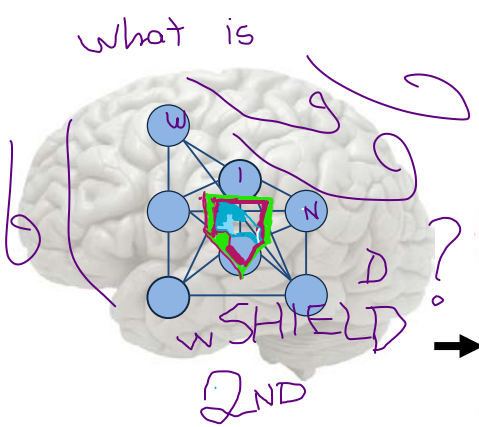
© Fotosearch.com

Engage neuromodulatory circuitry

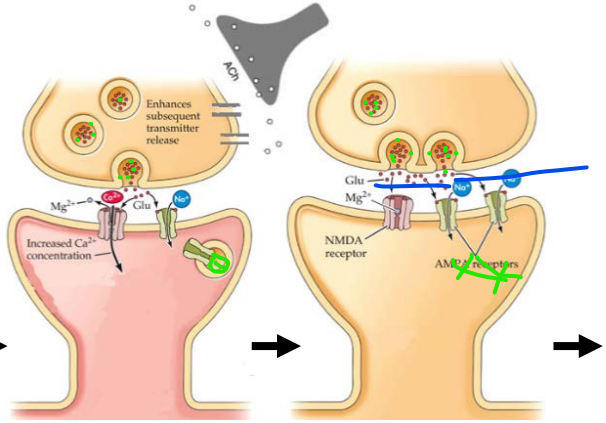


Result:
Train personnel **faster** & with **superior** cognitive abilities

Skill learning and the brain

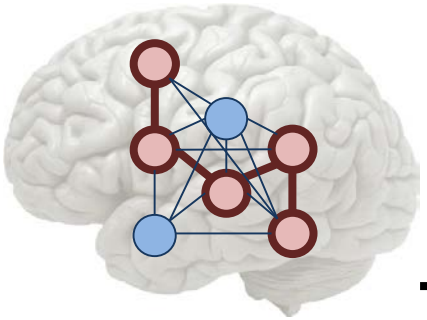


Initial Network



Neuromodulator Release
(e.g., acetylcholine, epinephrine, dopamine, seratonin)

Strengthened Synapse



Strengthened Neural Network

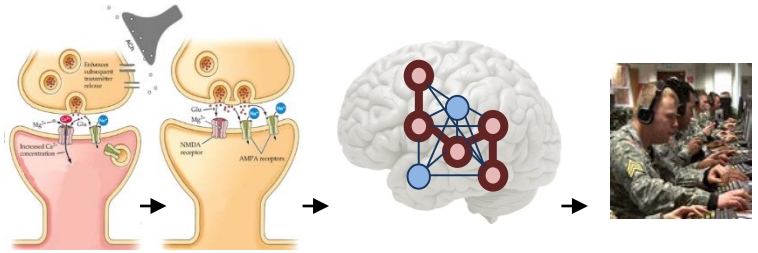
© US Army

Improved Skill Performance

Skill learning and the brain

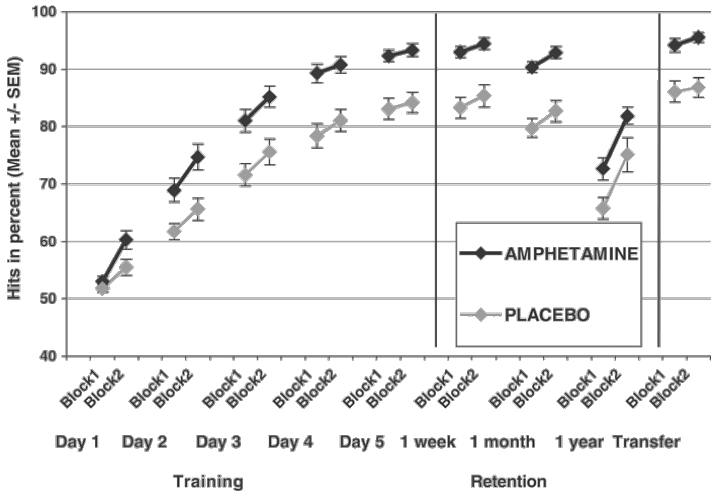
Pharmaceuticals

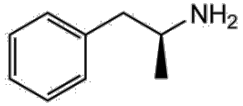
Enhances Learning?	Specific?	Invasive?	Side Effects?
Mixed - Some agents promote learning under specific circumstances	No	No	Yes, such as addiction, cardiac, and respiratory effects



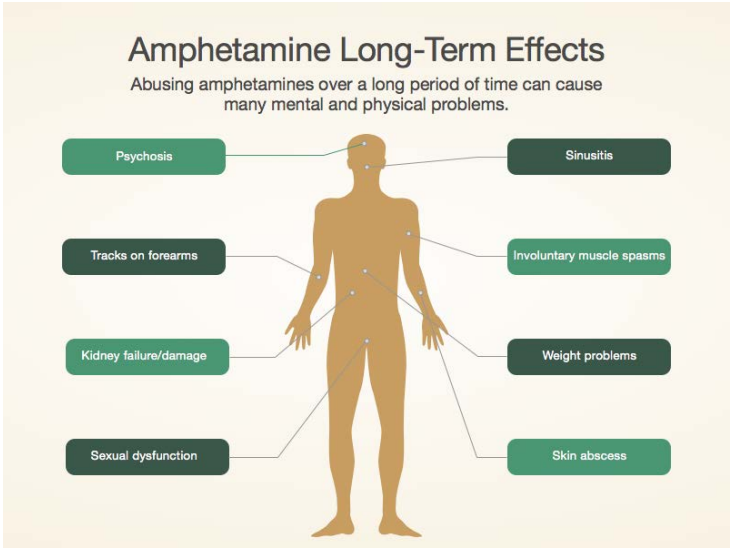
NT Release → Strengthened Synapse → Strengthened Network → Improved Skill Performance

Language transfer from visual to spoken material





d-amphetamine

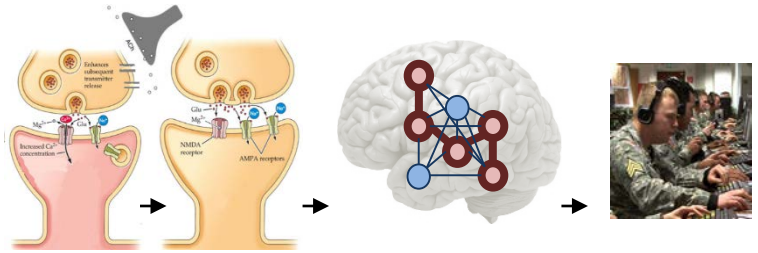


Breitenstein et al., 2004

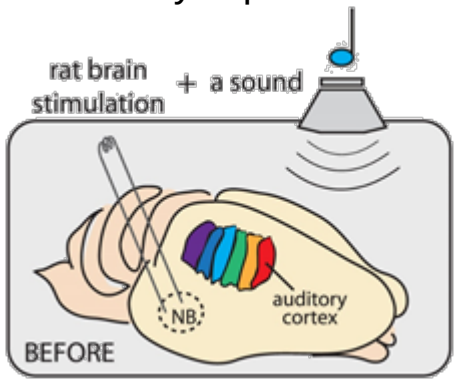
Skill learning and the brain

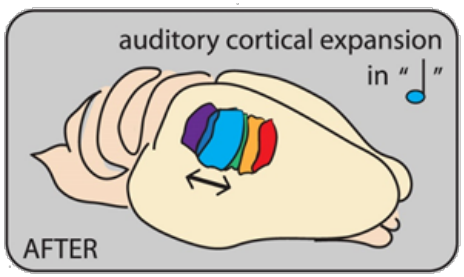
Deep Brain Stimulation

Enhances Learning?	Specific?	Invasive?	Side Effects?
Yes	Specificity depends on device	Requires implantation into brain	Surgical complications, off-target effects

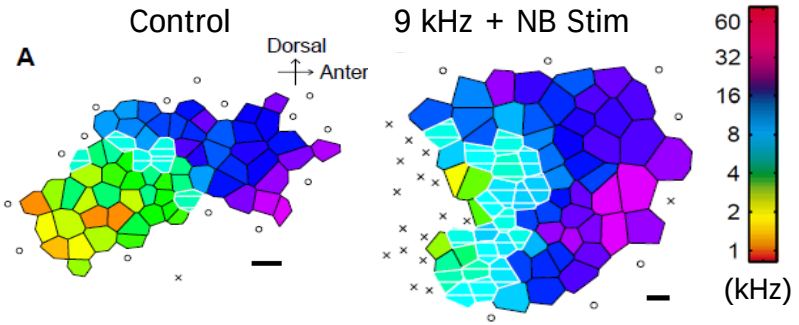


Paired Brain Stimulation and Sensory Exposure:





Increased representation of paired tone in auditory cortex:

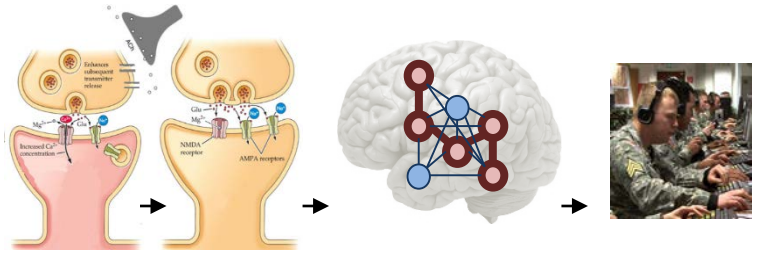


Kilgard et. Al., 1998

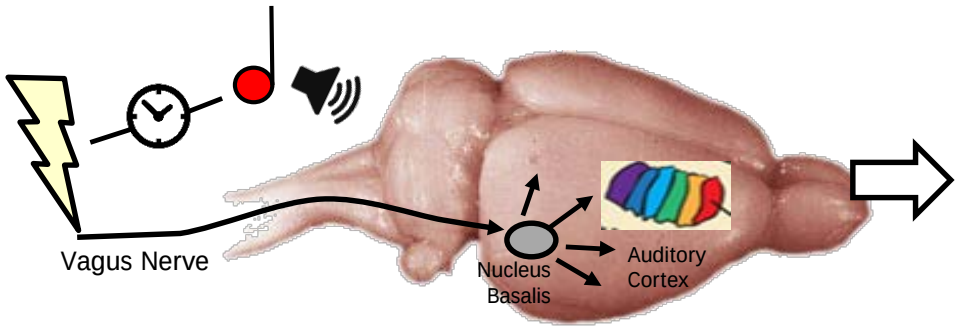
Skill learning and the brain

Invasive PNS Stimulation

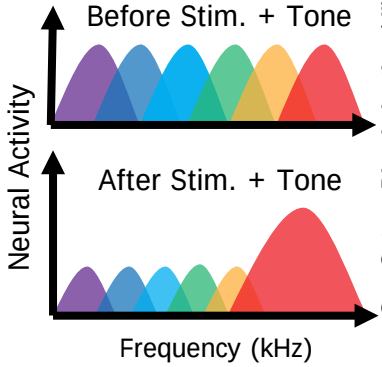
Enhances Learning?	Specific?	Invasive?	Side Effects?
Yes	Yes	Yes	Yes, minor



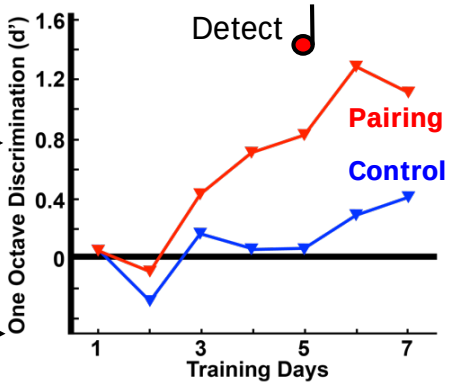
Paired Nerve Stimulation and Sensory Exposure:



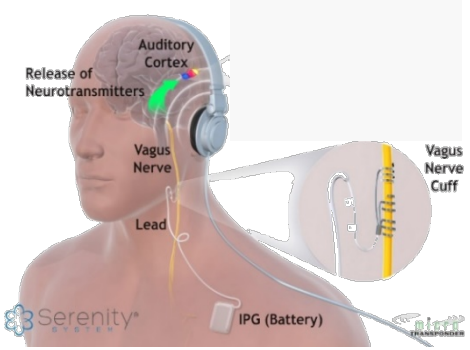
Neural Changes:

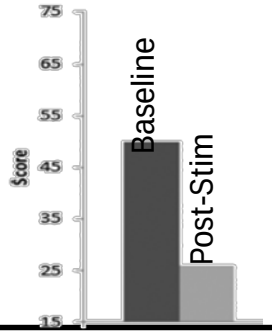


Behavioral Improvement:



Tinnitus Rehab in Humans:



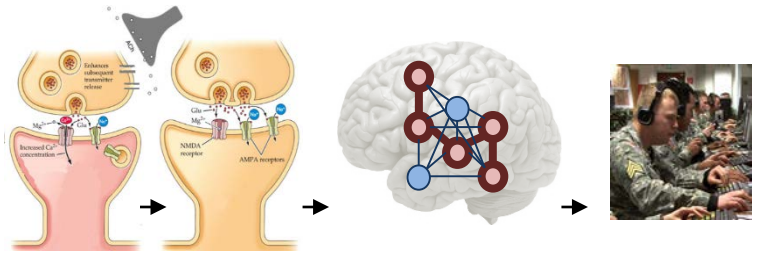


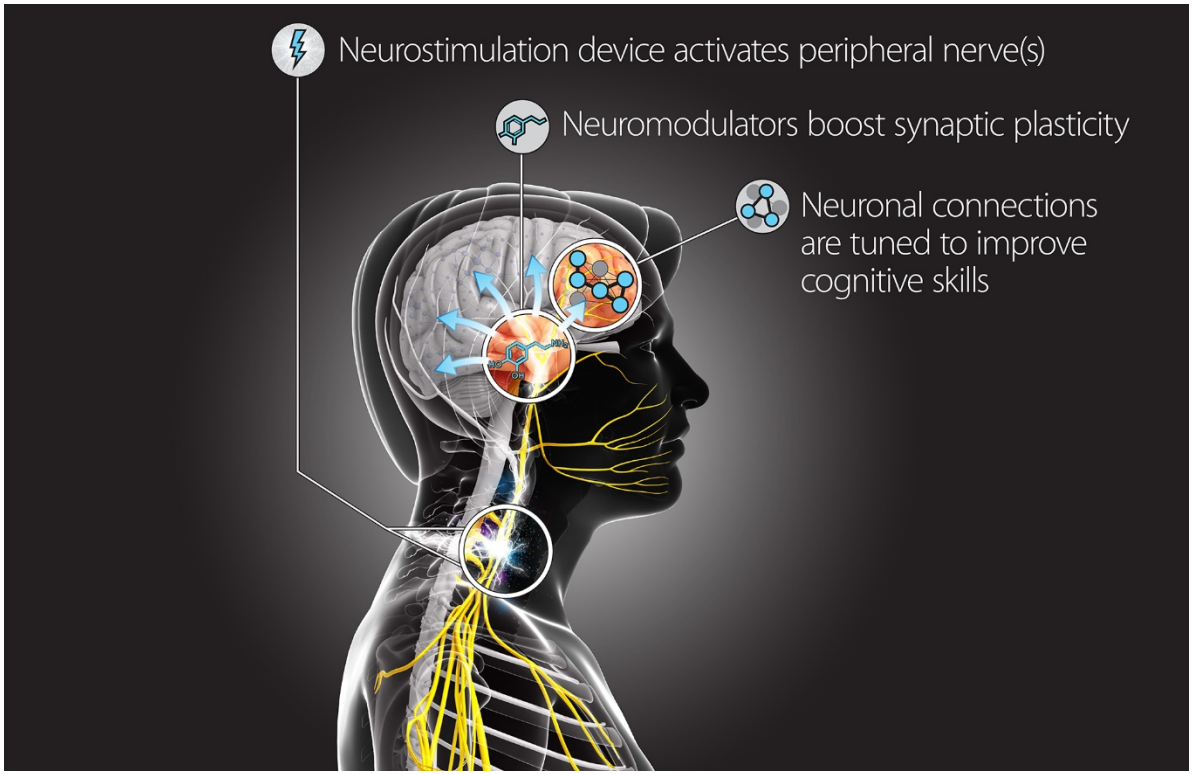
Shetake et. Al., 2012; De Ridder et al., 2015

Skill learning and the brain

Training + Non-Invasive PNS Stimulation

Enhances Learning?	Specific?	Invasive?	Side Effects?
Yes	Yes	No	No





General Objectives

1) Elucidate the anatomical and functional map(s) of the peripheral and central nervous system circuitry that regulates synaptic plasticity in the brain

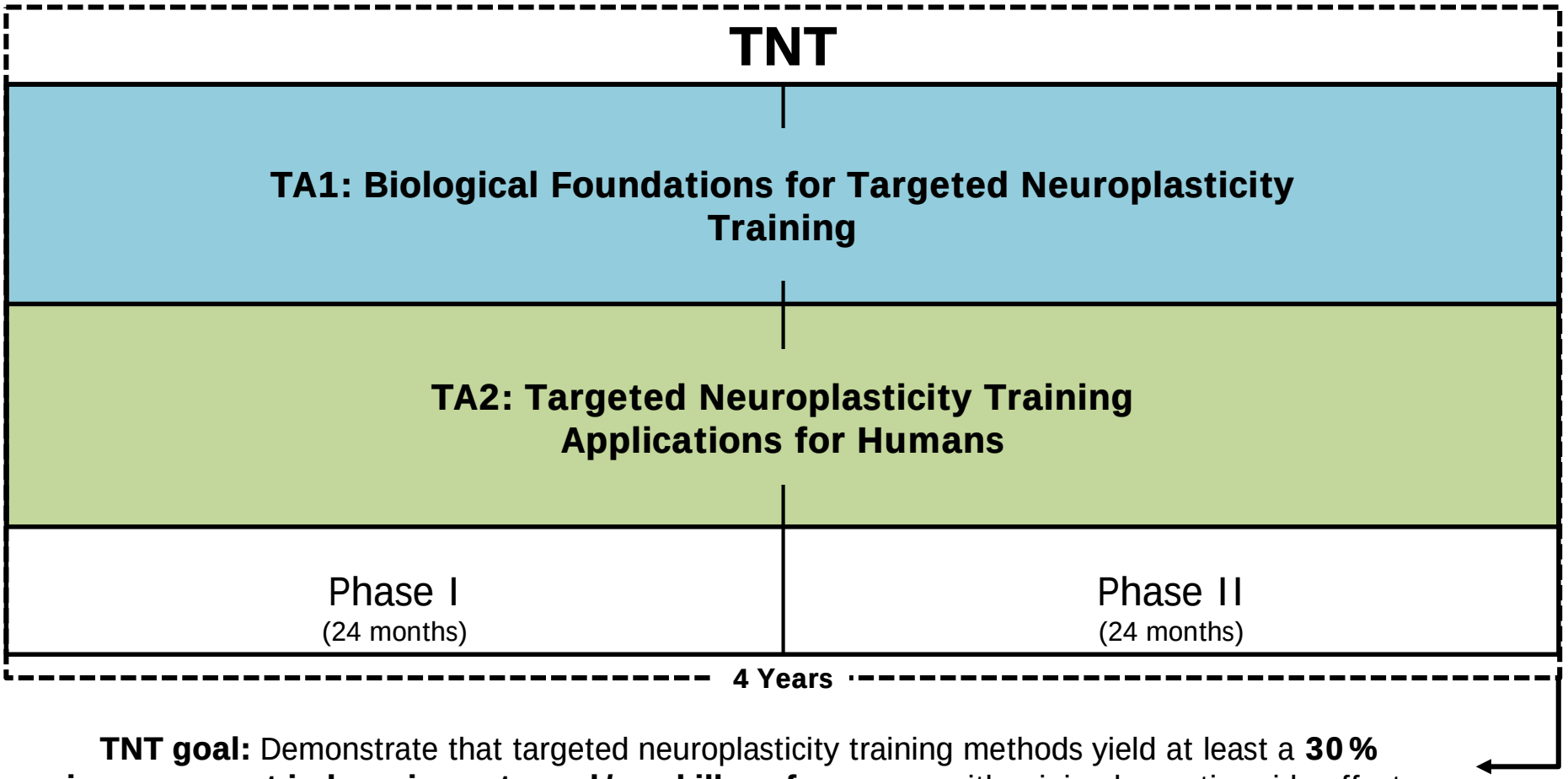
2) Demonstrate effects of peripheral neurostimulation on cognitive skills and the brain activity supporting those skills

3) Optimize noninvasive stimulation methods and training protocols for long-term retention without negative side effects

By the end of the 4-year TNT program:

Demonstrate that targeted neuroplasticity training methods yield at least a **30% improvement in learning rate and/or skill performance** with minimal negative side effects

Program Structure



TNT goal: Demonstrate that targeted neuroplasticity training methods yield at least a **30%** **improvement in learning rate and/or skill performance** with minimal negative side effects

End-of-Phase goals set by DARPA (see BAA and following slides)
Intermediate milestones set by performer and should be identified within proposal

TA1: Biological Foundations for Targeted Neuroplasticity Training

TA1 Primary objective: perform hypothesis-driven research to measure and demonstrate effects of peripheral neurostimulation in promoting plasticity, and assess quantitative changes in neurophysiology and behavior

Phase I Goals

Research Objectives	Milestones and Deliverables
Demonstrate that peripheral neurostimulation promotes synaptic plasticity by measuring changes in neural activity and neurochemicals in brain.	Provide data validating proposed hypotheses regarding functional and anatomical map(s) of circuitry between peripheral nerve and CNS structures. Input/output response profiles for peripheral neurostimulation and plasticity modulation in CNS.
Demonstrate acute effects of targeted neuroplasticity training on brain neurophysiology and learning rate and/or skill performance at least 15% greater than control.	Provide data demonstrating quantified changes in task performance (e.g., accuracy, speed) and neural network physiology (e.g., neural tuning functions and functional connectivity) with training.
Test for off-target effects of peripheral neurostimulation and training.	Provide stimulation parameter map for identified side effects.

TA1: Biological Foundations for Targeted Neuroplasticity Training

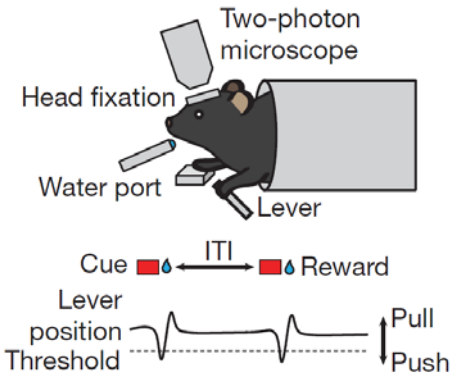
TA1 Primary objective: perform hypothesis-driven research to measure and demonstrate effects of peripheral neurostimulation in promoting plasticity, and assess quantitative changes in neurophysiology and behavior

Phase II Goals

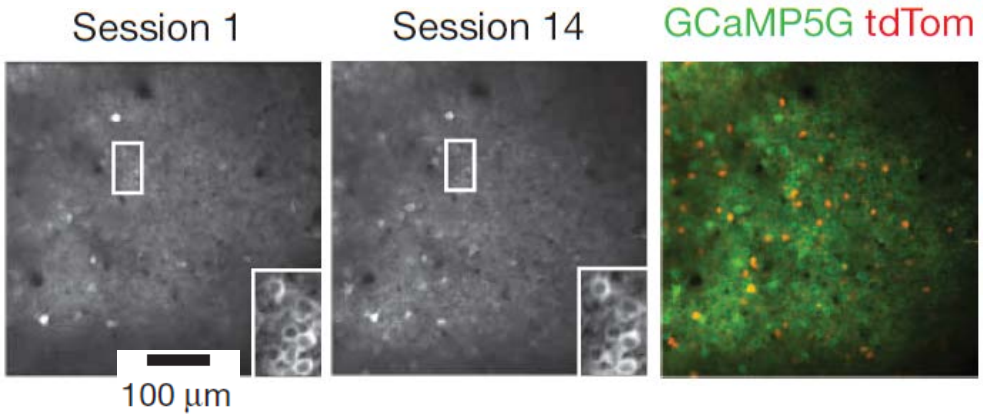
Research Objectives	Milestones and Deliverables
Demonstrate chronic effects of targeted neuroplasticity training on neurophysiology and learning rate and/or skill performance at least 30% greater than control, including measures of long-term retention of trained skills.	Provide data demonstrating quantified changes in task performance (e.g., accuracy, speed) and neural network physiology (e.g., neural tuning functions and functional connectivity) over training periods that span days or weeks and retention evaluated >30 days after training.
Optimize stimulus protocols in animal models to minimize negative side effects.	A peripheral neurostimulation and training protocol that exhibits minimal side effects in animal models.

Large-scale neural recording and learning studies

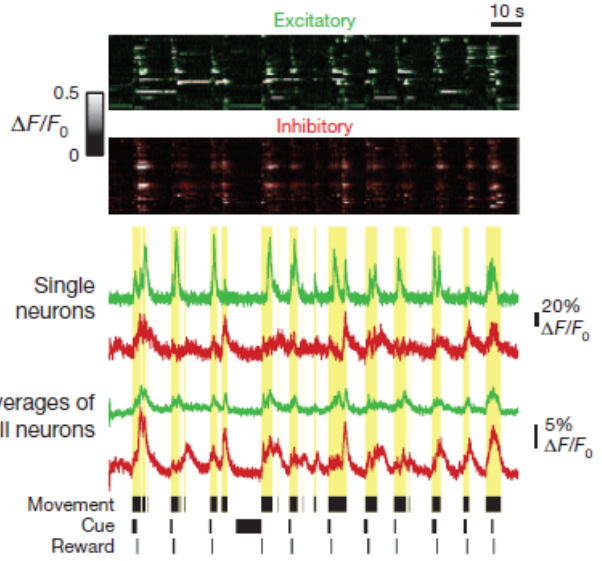
Motor learning task



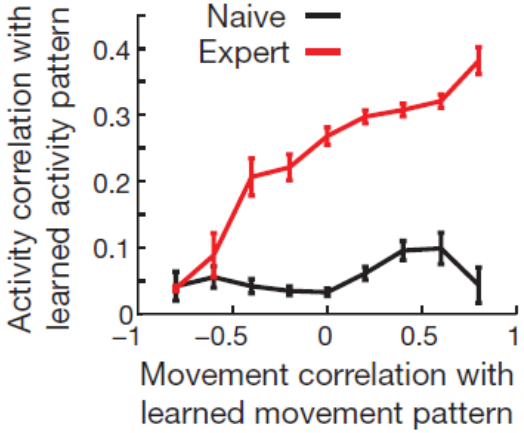
Calcium imaging of neurons in motor cortex

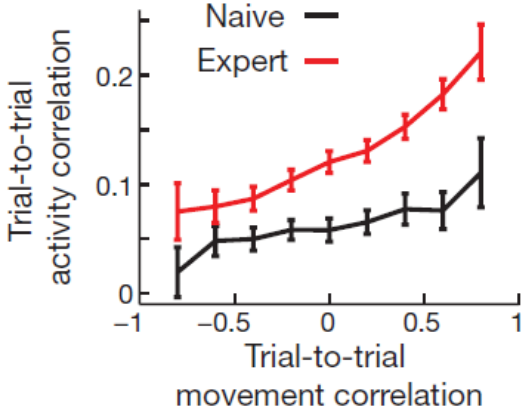


Analysis of neuronal activity



Coordinated evaluation of neuronal activity and task learning





Peters et. al., Nature 2014

TA2: Targeted Neuroplasticity Training Applications for Humans

TA2 Primary objective: Develop, demonstrate, and validate cognitive-skill training applications for humans that leverage noninvasive peripheral neurostimulation to promote synaptic plasticity.

Phase I Goals

Research Objectives	Milestones and Deliverables
Identify mechanisms for modulating neuroplasticity in humans with noninvasive peripheral neurostimulation devices.	Provide data validating proposed hypotheses regarding specific peripheral nerve targets for stimulation and effects on synaptic plasticity, brain function, and learning rates.

TA2: Targeted Neuroplasticity Training Applications for Humans

TA2 Primary objective: Develop, demonstrate, and validate cognitive-skill training applications for humans that leverage noninvasive peripheral neurostimulation to promote synaptic plasticity.

Phase II Goals

Research Objectives	Milestones and Deliverables
Refine peripheral neurostimulation and training protocols to ensure easy and reliable operation with minimal negative side effects.	A peripheral neurostimulation device and training protocol with reliable indicators of target nerve engagement and empirical data demonstrating minimal side effects on physical and cognitive functions.
Evaluate benefits of targeted neuroplasticity training with goal of demonstrating learning rate and/or skill performance at least 30% above control.	Provide performance data from randomized, controlled study comparing learning rates and retention between targeted neuroplasticity training and unstimulated controls.

Program Structure

Performer responsibility:
Demonstrate that your approach reduces training time in a lab setting

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© stevenlprime.ca

DARPA responsibility:
Find appropriate DoD partners to pursue implementation in the field

© US Army

Scope

	IN SCOPE	OUT OF SCOPE
Stimulation Approach	Technologies targeting the peripheral nervous system	Technologies targeting the central nervous system (including, but not limited to, tDCS, tACS, tRNS, TMS, DBS)
Targeted Skills	Perception, comprehension, decision making, motor control, and many others	Memory
Application space	DoD-relevant training in healthy adults (including, but not limited to, foreign language learning, TOC control, intelligence analysis, cryptography)	Rehabilitation and other clinical applications

Use of **NONINVASIVE** technologies is required.
Use of **INVASIVE** technologies for comparison is encouraged.

Use of **COTS technology** is expected. Development of novel devices is discouraged.

Proposals and Teaming

- Proposal Due Date: **June 2, 2016**
- Proposals must address TA1 and TA2 **in full**

Teaming

It is anticipated that teaming will be necessary to cover the wide range of animal and human tasking required in this program

Tips:

1) Listen to presenters during today's "intro blitz" sessions, where attendees will briefly present their expertise and capabilities

2) Utilize the TNT teaming website: https://team.sainc.com/TNT/home.aspx.

3) Reach out to colleagues and collaborators

BAA Inbox and FAQ

- Direct ***ALL*** questions and communication to the BAA Inbox
  - DARPA-BAA-16-24@darpa.mil
  - Dr. Weber, any member of his team, or any member of the scientific review panel will not directly communicate with a potential proposer regarding BAA-16-24; all communication will be conducted through the BAA Inbox
  - Dr. Weber and the BAA Inbox cannot provide feedback or guidance on any aspect of your proposal, they can only clarify the content of BAA-16-24
- BAA Inbox FAQ
  - DARPA will post a consolidated FAQs on a regular basis
  - To access the posting go to:
    - https://www.fbo.gov/spg/ODA/DARPA/CMO/DARPA-BAA-16-26/listing.html
  - Submit your question(s) by E-mail to DARPA-BAA-16-24@darpa.mil at least 15 days before the proposal submission deadline

Advice

- Read the BAA, carefully – and respond accordingly.
  - Some instructions are specific – “required” and “must”
  - Most of the instructions are non-specific – you decide on what is the best possible science to support the objectives of the program
  - Be honest about risks and demonstrate thoughtful consideration for how to mitigate those risks.

- Ask for clarification as needed. FAQs will be updated regularly.

- Take advantage of today’s opportunities to meet potential teammates and ask questions

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