



# AFRL

## OPTIMIZING COGNITIVE PERFORMANCE IN THE OPERATIONAL ENVIRONMENT WITH NEUROMODULATION

LINDSEY MCINTIRE.

711<sup>TH</sup> HUMAN PERFORMANCE WING 8/3/2026



# Disclaimer

The opinions expressed herein are my own and do not reflect the official policy or position of the Department of the Air Force, the Department of War, or the U.S Government.

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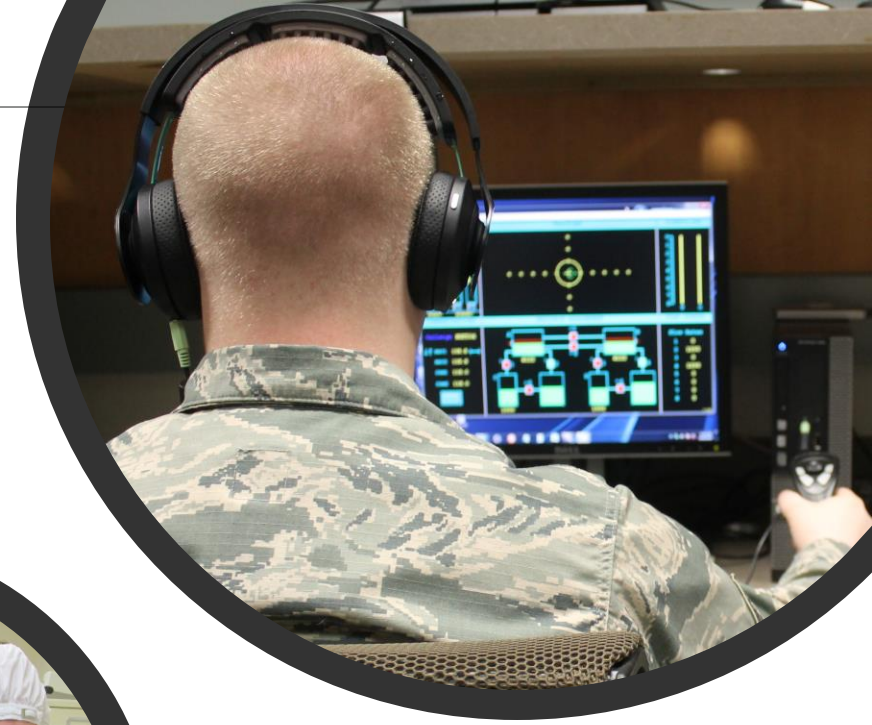
# Non-Disclosure

Lindsey McIntire has no conflicts to report.



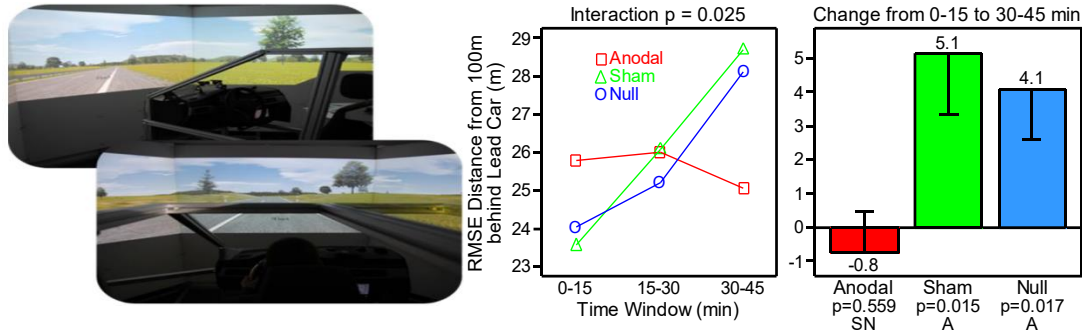
# Neuromodulation

- Neuromodulation techniques/technologies are used to modulate specific parts of the brain to influence brain activity.
- Variety of methods are used invasively (deep brain stimulation, implanted VNS) and non-invasively (tES, PBM, tFUS) to treat a wide variety of clinical disorders that range from epilepsy, psychiatric, neurogenerative, sleep, pain, etc.
- AFRL has been researching non-invasive methods to enhance cognitive performance since 2008.

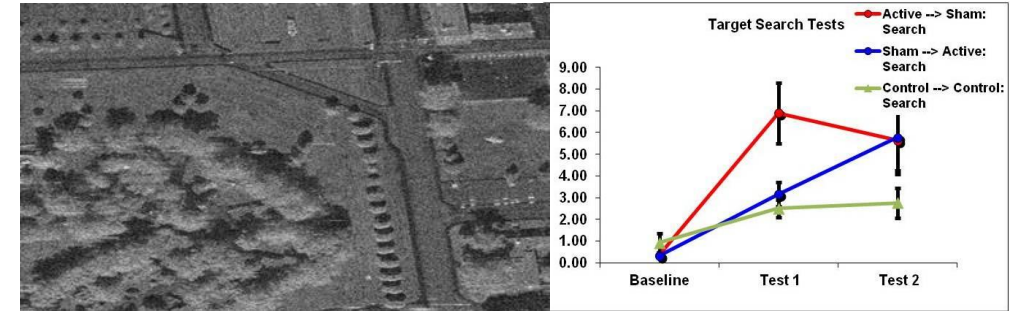


# Historically found transcranial direct current stimulation (tDCS) enhanced:

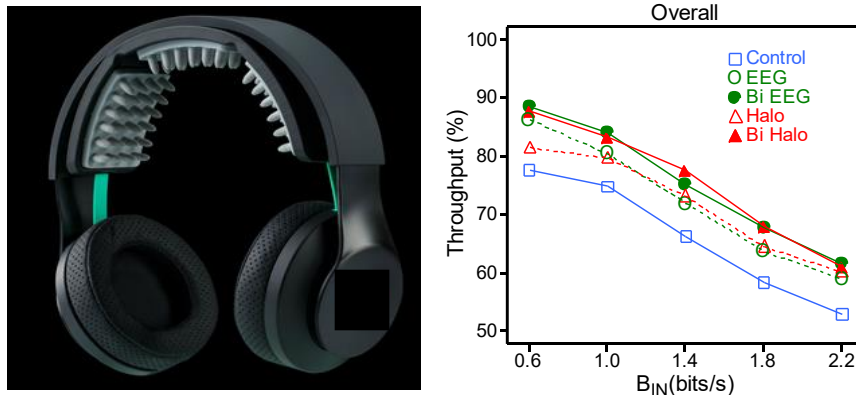
## Vigilance/Attention



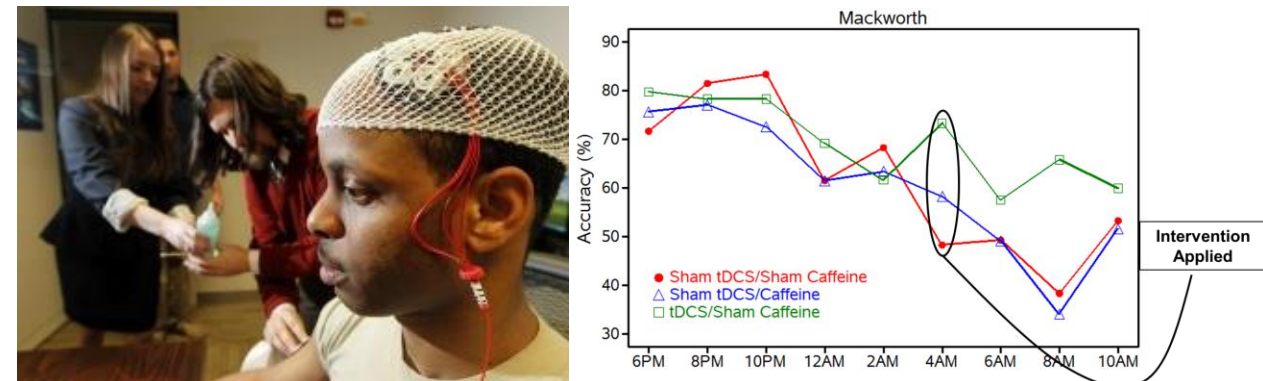
## ISR Learning



## Multitasking



## Fatigue Resistance



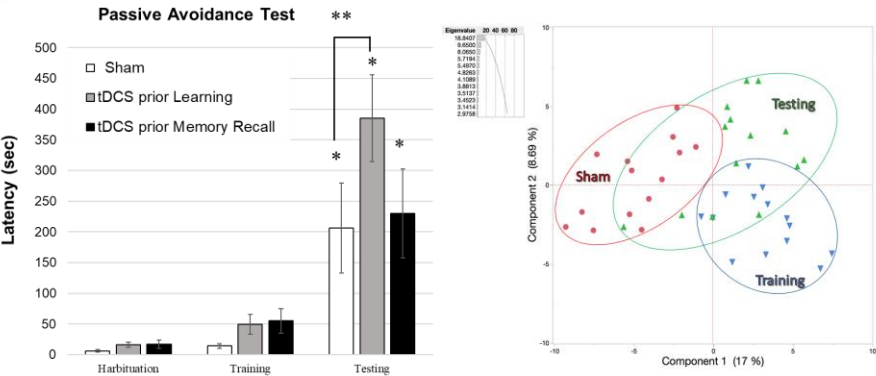
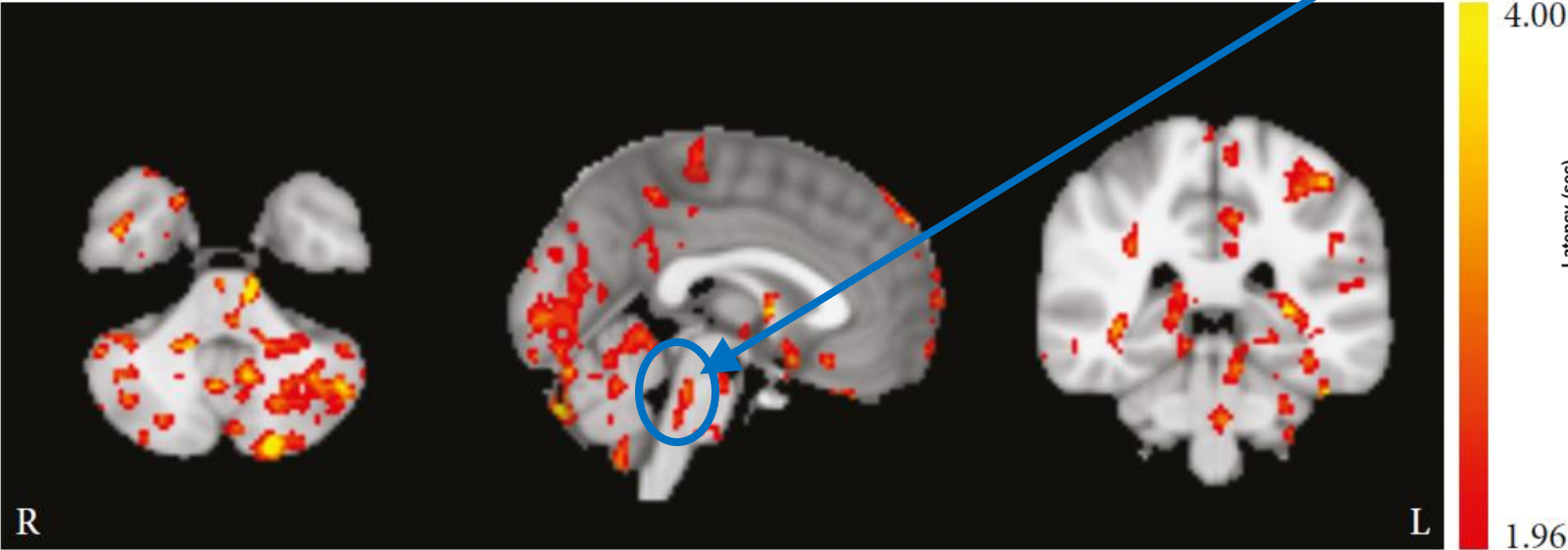
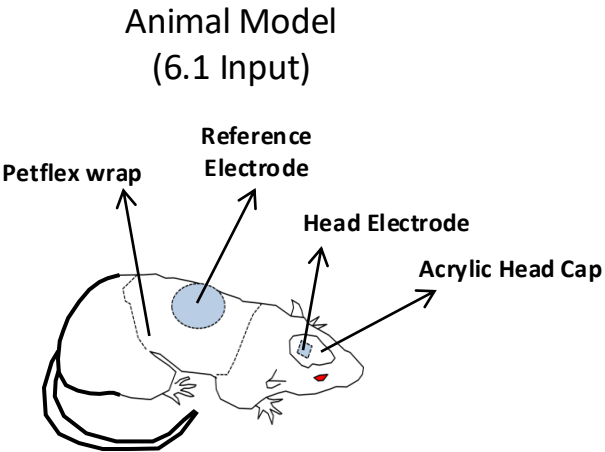
# Neurophysiology Results-these technologies are modifying parts of the brain that control attention, arousal, learning, and memory.

Research Article

## Repetitive Transcranial Electrical Stimulation Induces Quantified Changes in Resting Cerebral Perfusion Measured from Arterial Spin Labeling

Matthew S. Sherwood<sup>1,2</sup>, Aaron T. Madaris<sup>1,2</sup>, Casserly R. Mullenger<sup>1</sup>, and R. Andy McKinley<sup>3</sup>

Locus Coeruleus



tDCS is capable of modifying hippocampal protein abundance in a manner that may promote learning and memory

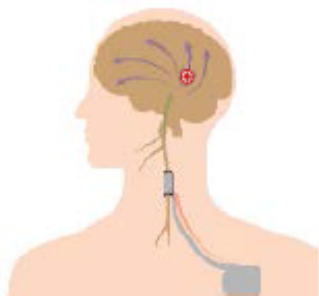


# Peripheral Nerve Stimulation

# Effects on Learning

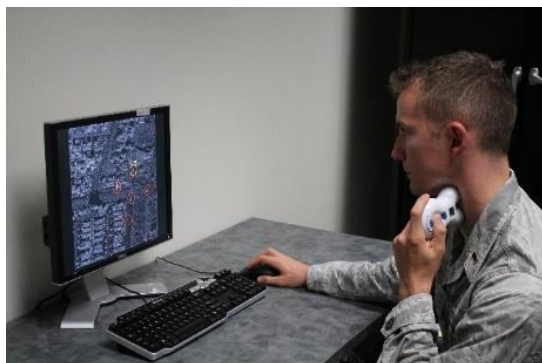
## Transcutaneous Vagal Nerve Stimulation (tVNS)

### Peripheral Nerve Stimulation



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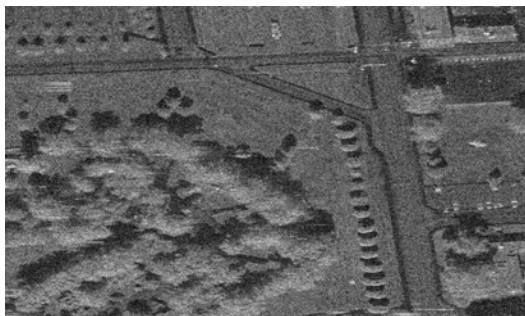
Engage neuromodulatory circuitry



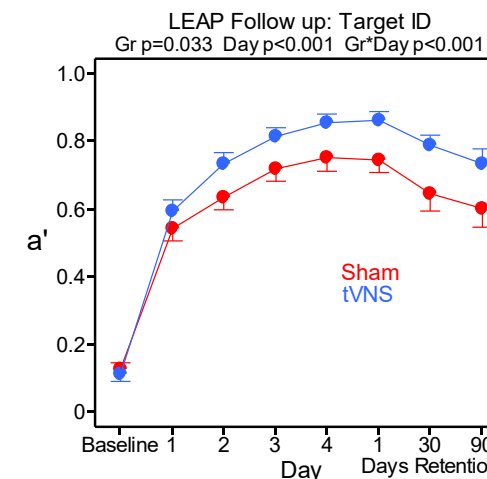
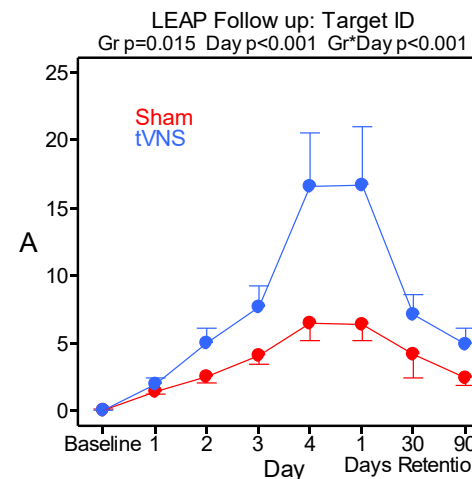
- LC involved in memory, attention, arousal, and wakefulness
- Shown to enhance memory retention



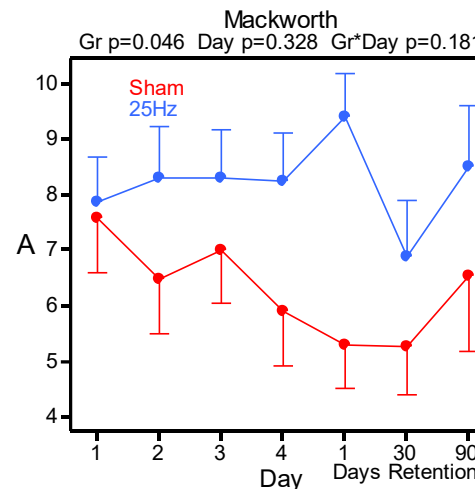
FDA Approved



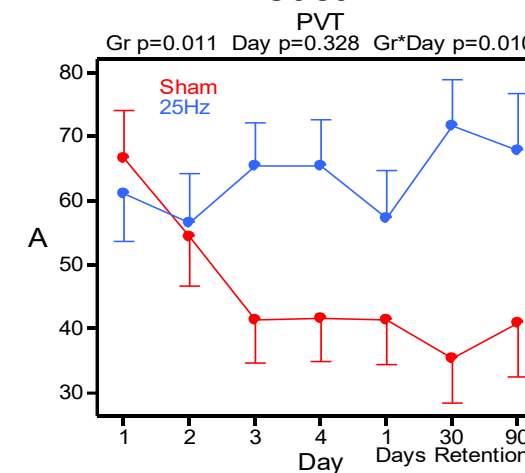
## Learning



## Attention



## Arousal



# Fatigue and tVNS (transcutaneous vagal nerve stimulation)



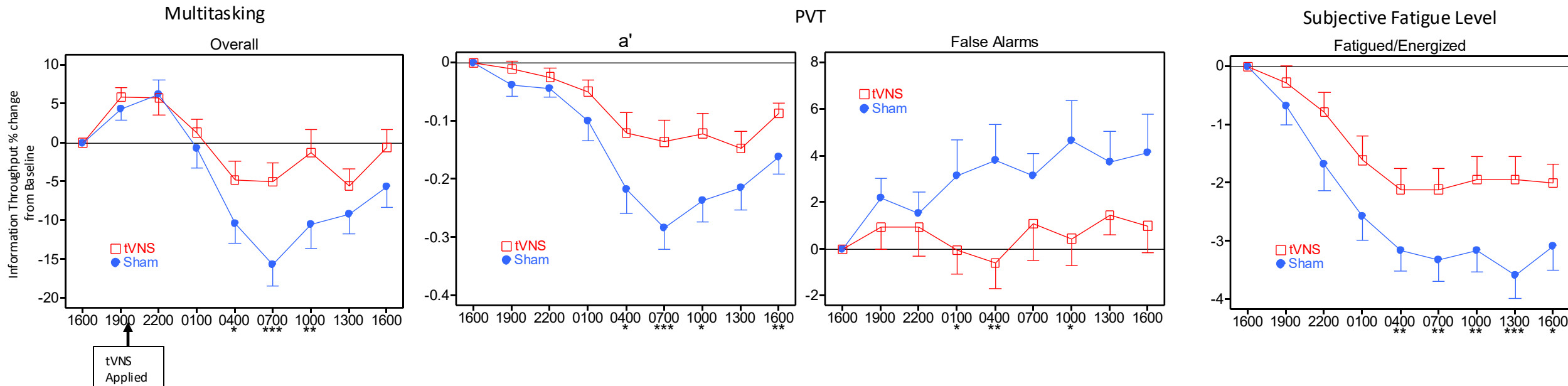
## Effects of cervical tVNS on Sleep Deprivation WPAFB, OH

- NASA is interested in novel technologies that can mitigate performance losses due to fatigue caused by sleep loss
  - Data collection complete (N = 40; 20 Active and 20 Sham subjects)
  - Stimulation applied at 7pm (13 hours into sleep deprivation period)
  - Baseline defined as 4pm (10 hours into sleep deprivation period)
  - Sleep deprivation period lasted 36 hours.
- Performance and mood sustained for up to 14 hours post stimulation.

Data published in:

**Nature Communications  
Biology**  
Journal

ORA

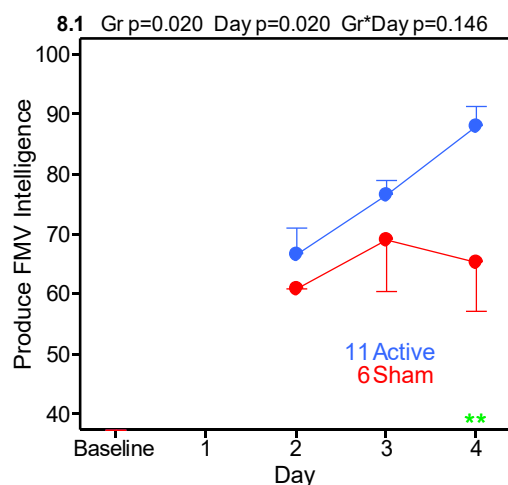
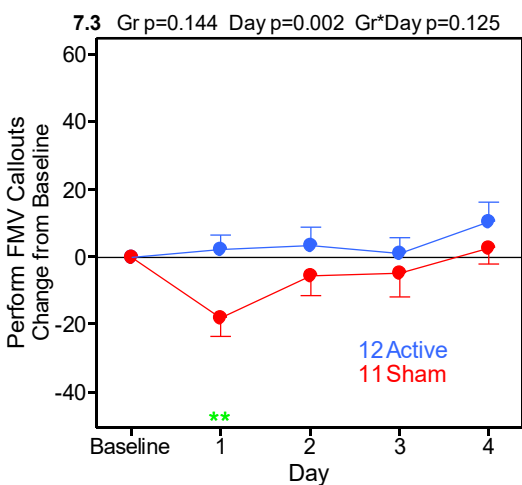




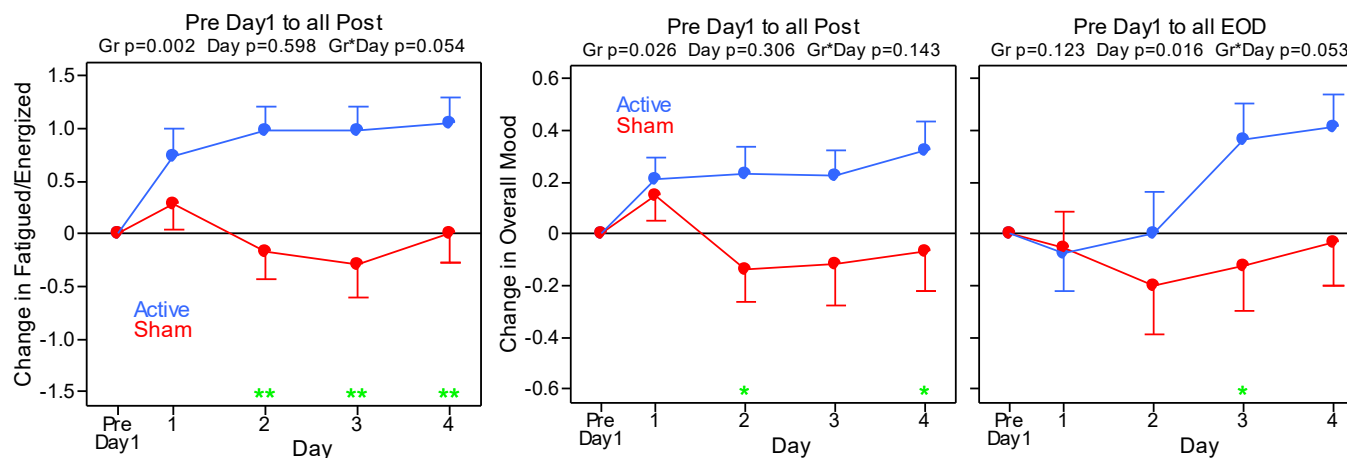
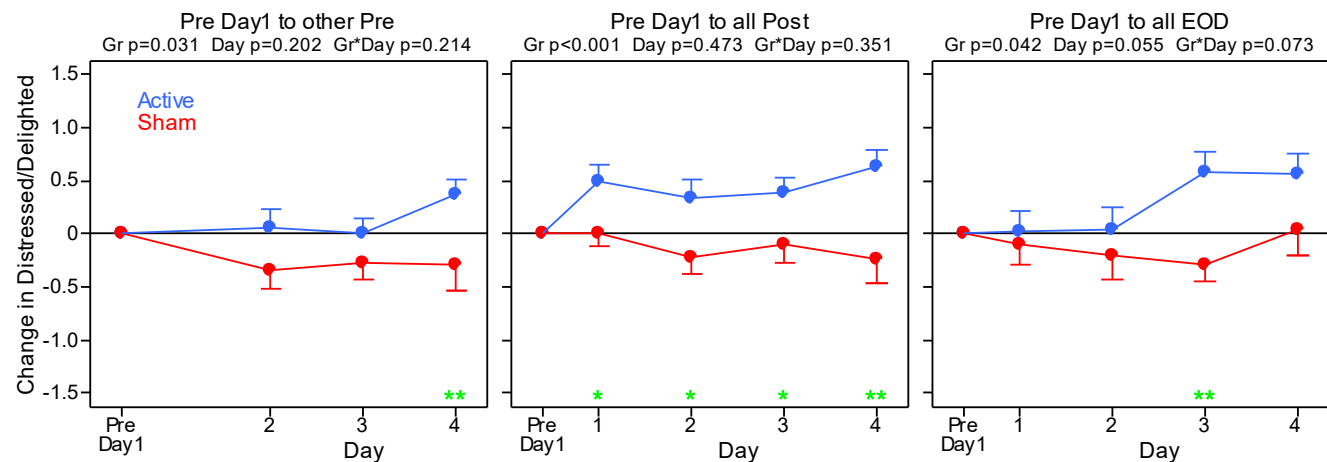
# AFSOC ISR Trainee Field Study



Instructor Assessments

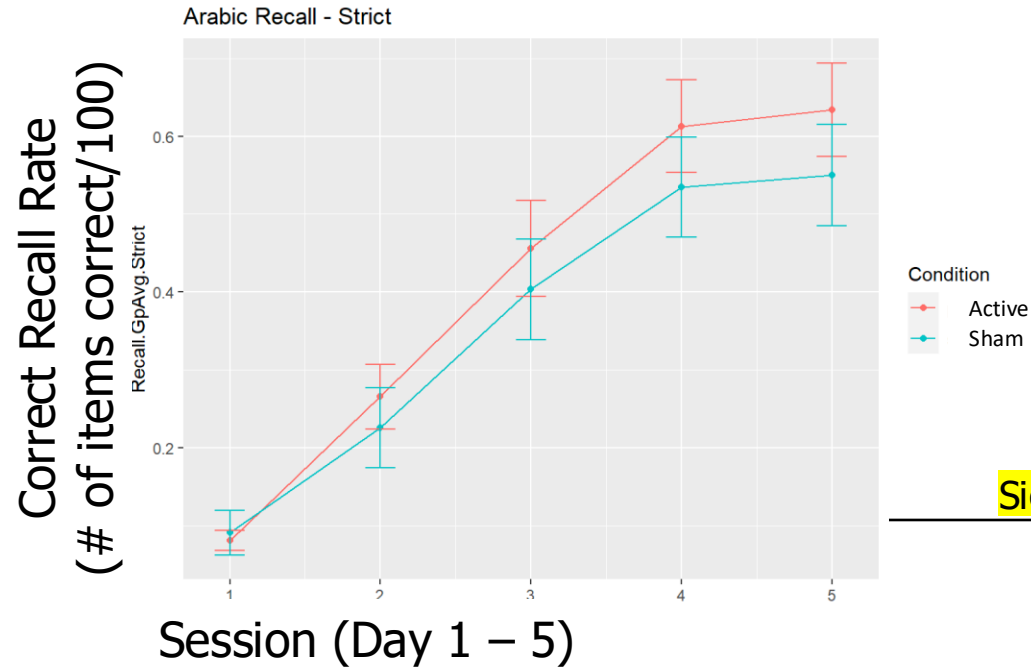


**Mood Results:** Less stressed, less fatigued and more energized, & overall more positive mood.



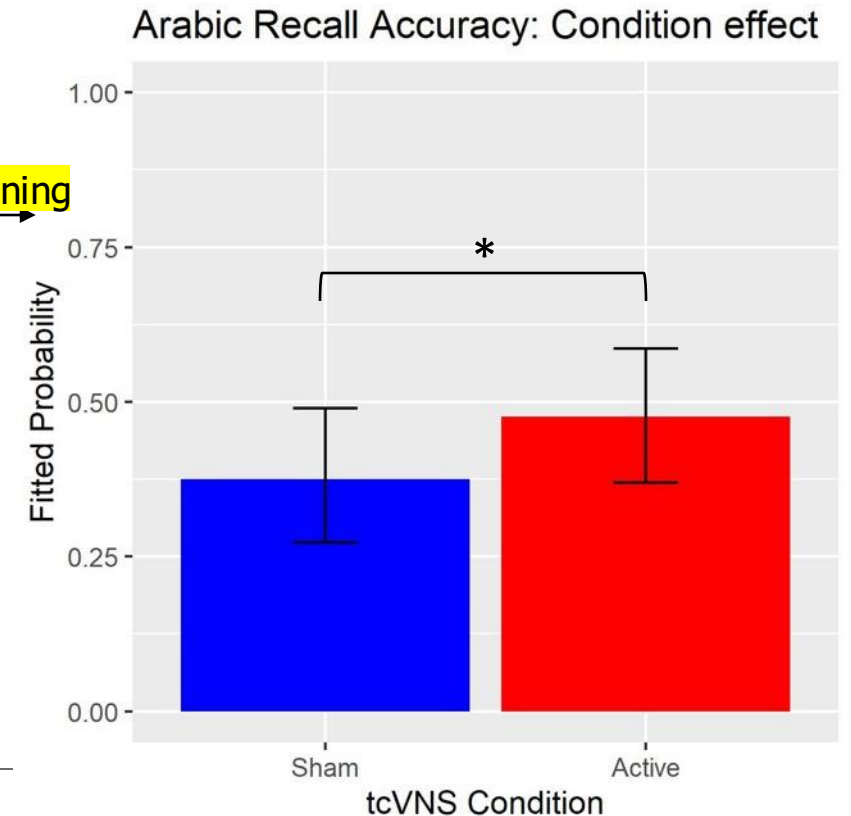


# Defense Language Institute (DLI) Field Study (Arabic)



| Fixed Effects                      | Estimate | SE    | z-value | p-value |
|------------------------------------|----------|-------|---------|---------|
| (Intercept)                        | -1.822   | 0.252 | -7.226  | < .001  |
| Baseline Recall Score              | 14.509   | 1.052 | 13.798  | < .001  |
| Session                            | 1.312    | 0.083 | 15.875  | < .001  |
| Condition (tVNS vs sham)           | 0.532    | 0.238 | 2.234   | .025    |
| Session x Condition (tVNS vs sham) | -0.116   | 0.096 | -1.202  | .229    |

**tVNS accelerated learning  
of Arabic vocabulary words  
by 20%**





# Air Traffic Control Trainees Study

# Methods-Air Traffic Control Trainees

- Desired N = 40 active, 40 sham in each course
- Current N = 31 active, 17 sham for Tower and 19 active, 12 sham for Radar
- Prior to Training for Tower Basic and Radar Basic
  - Informed Consent
  - Medical Screening
  - Train on device use and questionnaire
- Each Day of Study Participation during Tower Basic and Radar Basic Training
  - AM Testing-Prior to training for the day
    1. Mood Questionnaire
    2. Sensation Questionnaire
    3. tVNS (active or sham)
    4. Sensation Questionnaire
    5. Mood Questionnaire
  - Lunch Testing-Middle of the training day
    1. Mood Questionnaire
    2. Sensation Questionnaire
    3. tVNS (active or sham)
    4. Sensation Questionnaire
    5. Mood Questionnaire
  - PM Testing-End of training day
    1. Mood Questionnaire

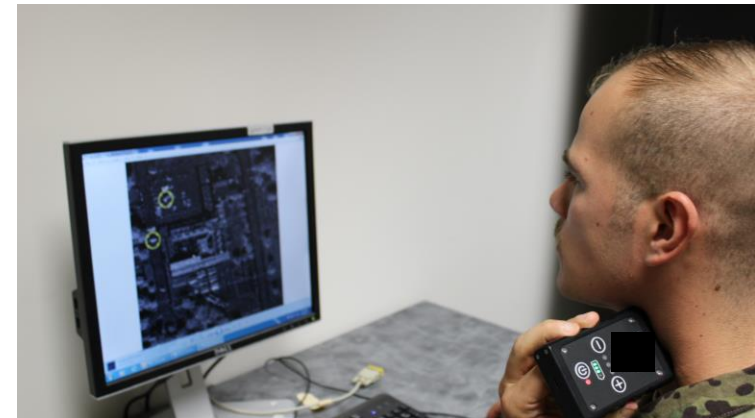


\*Photo curtesy of 334 TRS

# Equipment

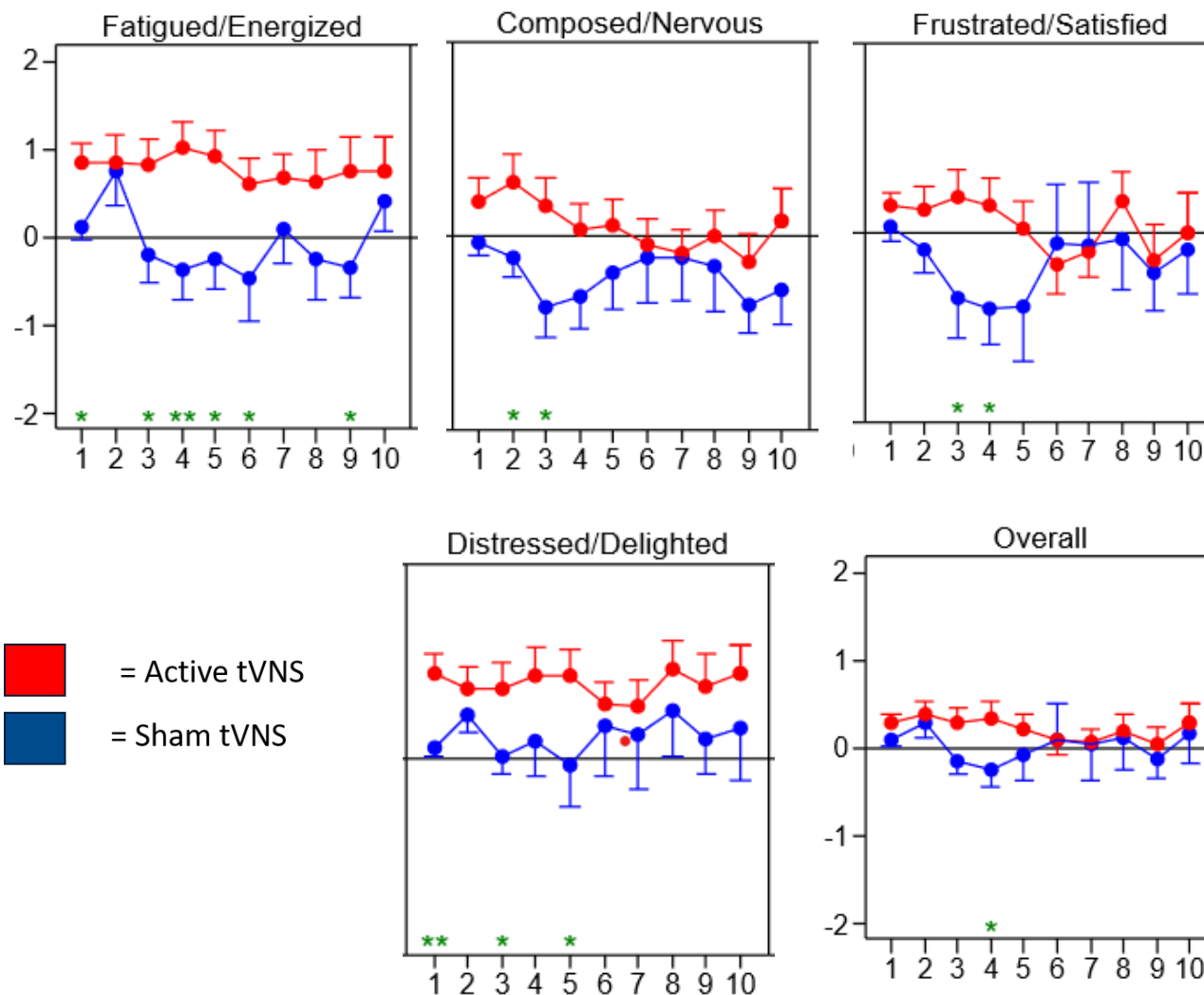
## TAC-STIM

- Handheld tVNS device
  - Developed and manufactured by electroCore®, Inc
- Specifications
  - Two electrodes used for stimulation
  - Non-invasive electrical current pulsed at 25 Hz through the skin to the cervical vagal nerve
- Stimulation protocol
  - 4 minutes of stimulation on left side of the neck before class and during lunch break.
- Active vs. Sham
  - Device housing is visibly identical
  - Sham device produces similar clicking sounds and tactile vibrations

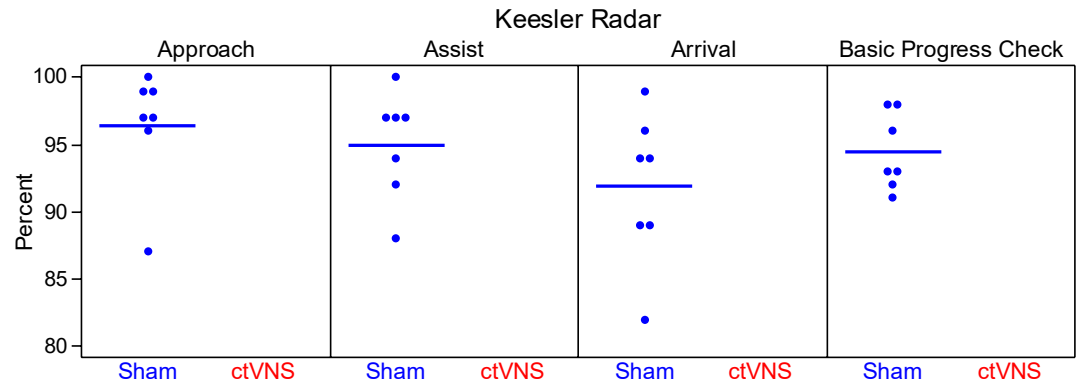




|                                                                            | 1                        | 2                        | 3                        | 4                        | 5                        | 6                        | 7                        |                                                                             |
|----------------------------------------------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-----------------------------------------------------------------------------|
| Focused (paying attention; deep concentration)                             | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Distracted (having attention diverted; unable to concentrate)               |
| Excited (being emotionally aroused; stirred)                               | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Calm (composed; tranquil)                                                   |
| Distressed (anxiety or mental suffering; experiencing physical discomfort) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Delighted (filled with great pleasure or joy)                               |
| Able (having sufficient power or resources to accomplish the current task) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Unable (lacking mental or physical capability to complete the current task) |
| Confused (being unable to think clearly; incomprehension)                  | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Not Confused (understanding the task at hand; thinking clearly)             |
| Tense (in a state of mental, emotional or nervous strain)                  | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Relaxed (free from strain or tension; easy and informational in manner)     |
| Happy (being satisfied or joyous)                                          | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Sad (experiencing feelings of sorrow or gloom)                              |
| At Ease (comfortable or relieved; ready to perform)                        | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Restless (being unable to relax or be still)                                |
| Optimistic (expecting a favorable outcome)                                 | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Pessimistic (a tendency to stress the negative)                             |
| Composed (calm)                                                            | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Nervous (easily agitated or distressed)                                     |
| Tranquil (free from anxiety or tension)                                    | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Angry (uneasy or anxious)                                                   |
| Frustrated (unable to accomplish a task; discouraged)                      | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Satisfied (filled with content; assured)                                    |
| Fatigued (tired; overcome with physical or mental exhaustion)              | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Energized (invigorated; prepared for activity)                              |
| Contented (satisfied with things as they are)                              | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Dissatisfied (disappointed; doubtful)                                       |
| Worried (uneasy or concerned about something)                              | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | Peaceful (in a state of tranquility)                                        |

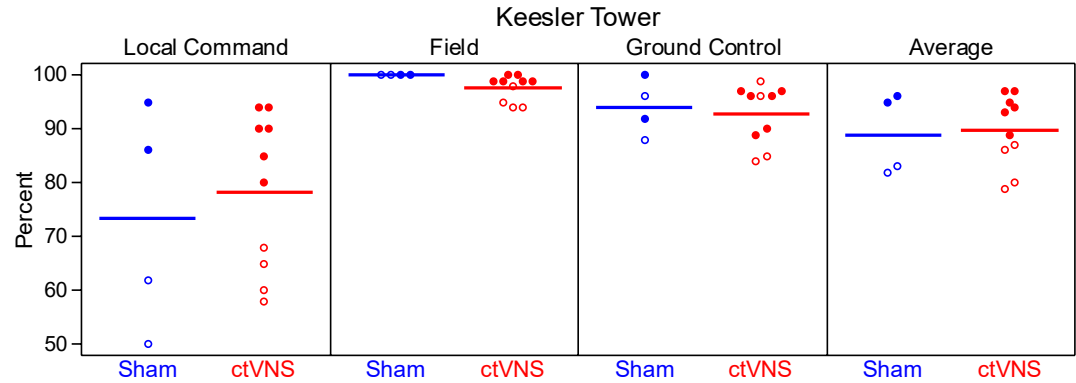


- Due to limited n-size we combined the mood ratings from both classes for this analysis (N= 50 active, 29 sham) and used only the first 10 days of data since the classes are different lengths.



= Active tVNS

= Sham tVNS





## Discussion/Conclusions

- tVNS appears to have an immediate effect on mood. Trainees immediately reported feeling more energized, less nervous, less stressed, less frustrated, and overall in a more positive mood.
- The effects on mood lasted several days in the early part of training. After about the first 5 days, the effect goes away. It appears the training is most stressful in the first few days as trainees are adjusting to the course. After about the first week, sham returns to baseline mood levels similar to before the course started.
- The effect on subjective fatigue levels appears to last the duration of the use of the device with those receiving active tVNS reporting enhanced alertness during training days compared to sham.
- At this time, we do not have enough instructor evaluations to draw any conclusion on how tVNS might effect learning or course performance.
- This field evaluation coupled with laboratory evidence shows that tVNS is not only capable of enhancing learning but can also assist the warfighter's ability to handle stress and extend their performance for longer periods of time.
- Future research should focus on the utility of other neuromodulation devices and other learning applications.
- While our lab has primarily focused on cognitive performance enhancement with neuromodulation technologies, it is a dual-use technology and we are interested in exploring medical applications.



# QUESTIONS?

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# Long-Term Chronic Use

Implanted VNS – Over 100K patients; 1K have had implant for over a decade

- Activated 480 times per day (more stims in one week than TAC-STIM/gammaCore in a year)
- No long-term adverse events, and no decrease of effect in epilepsy and depression

Research and clinical trials on gammaCore, nVNS device used for treating cluster headaches and migraine, suggest that **long-term adverse events are generally not a concern**. The device is considered safe and well-tolerated.

- Current gammaCore Clinical Users number over 78,000 (4-5 years of chronic/daily use) – **ZERO** newly emerging adverse events/effects

## Key findings regarding gammaCore safety:

- Mild and transient side effects: Most reported side effects are mild, occur during device use, and disappear shortly after each treatment session.
- No discontinuations due to adverse events: In studies, no participants discontinued gammaCore use because of side effects.

**Common side effects:** The most frequently reported side effects related to device use are localized skin tingling or irritation, burning, muscle soreness, and/or redness at the application site. These typically resolve quickly after use.

- Similar safety profile to sham: The safety profile for gammaCore was similar to sham (placebo) treatments in clinical trials, suggesting a favorable safety profile.
- **No serious device-related adverse events:** No serious adverse events were considered device-related in clinical studies.
- Can be used with medication: GammaCore can be used in combination with other drug treatments without any known interactions



# Clinical Trials of GammaCore

| Indication                            | No. of Patients | Status                              | Key Endpoints                                               | Institution(s)                   |
|---------------------------------------|-----------------|-------------------------------------|-------------------------------------------------------------|----------------------------------|
| Acute Treatment of Stroke (VENUS)     | 68              | <i>Published, Brain Stimulation</i> | Safety, Feasibility, Efficacy Signal                        | Hacettepe University + 8         |
| SAH Headache                          | 40              | Data H2 2023                        | Difference in Morphine Equivalent Dosage                    | Northwell                        |
| Acute Treatment of Ischemic Stroke    | 124/150         | Enrolling                           | Infarct volume, mRS, Safety, Feasability                    | Leiden University Medical Center |
| Acute Treatment of SAH                | 20              | Enrolling                           | Safety, Feasibility, Efficacy Signal                        | MGH                              |
| Acute Treatment of TBI (Pre-Clinical) | NA              | Published                           | Decrease in lesion size, improvement in neuropsych measures | University of New Mexico         |



# Medical Trials of GammaCore

Robust Mood Effects!

| Indication                 | No. of Patients | Status      | Key Endpoints                                          | Institution(s)               |
|----------------------------|-----------------|-------------|--------------------------------------------------------|------------------------------|
| PTSD in Veterans           | 88              | Enrolling   | Safety, Feasibility, Efficacy Signal                   | San Diego VA, UCSD           |
| PTSD due to TBI (Veterans) | 100             | Enrolling   | Imaging, Inflammation and Clinical outcomes            | Emory, GaTech                |
| PTSD – General (Veterans)  | 80              | Pending     | Clinical and Physiological outcomes                    | Emory, GaTech                |
| Opioid Use Withdrawal      | 100             | UH3 Awarded | Reduction in Subjective Opioid Withdrawal Scale (SOWS) | Emory, GaTech, Johns Hopkins |

**Granted “Breakthrough Device” Designation from FDA for Treatment of PTSD!  
Symptoms reduced by 31% compared to sham!!**