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The views, opinions and/or findings contained in this report are those of the author(s) and should not contrued as an official Department of the Army position, policy or decision, unless so designated by other documentation.

14. ABSTRACT

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| a. REPORT | b. ABSTRACT | c. THIS PAGE | | | Bart Krekelberg |
| UU | UU | UU | UU | | 19b. TELEPHONE NUMBER: 973-353-3602 |

# RPPR Final Report
as of 24-Jan-2019

Agency Code:

Proposal Number: 63868LS **Agreement Number: W911NF-14-1-0408**
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DUNS Number: 130029205 EIN: 226001086
**Report Date:** 01-Apr-2018 Date Received: 19-Jan-2019
**Final Report** for Period Beginning 01-Aug-2014 and Ending 01-Jan-2018
**Title:** Targeted Transcranial Electric Stimulation (Section II, A, 2, 8.4: Life Sciences, Neurophysiology & Cognitive Neuroscience)
**Begin Performance Period:** 01-Aug-2014 **End Performance Period:** 01-Jan-2018
**Report Term:** 0-Other
Submitted By: Bart Krekelberg Email: bart@vision.rutgers.edu
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**Distribution Statement:** 1-Approved for public release; distribution is unlimited.

**STEM Degrees:** 2 **STEM Participants:** 8

**Major Goals:** This project has two major goals.
First, we want to improve methods with which electrical stimulation can be targeted to specific parts of the brain. Second, we want to understand what happens at the neural level in an intact brain when electrical fields are applied.

**Accomplishments:** In terms of the first goal (improved targeting) - we fine tuned current flow models based on MRI images of the individual anatomy of a macaque, developed techniques to record intracranial fields in the macaque brain, and measured fields at a small sub-millimeter scale. These measurements provided the first evidence that intracranial fields are potentially large enough to modulate neural activity in the primate. In addition, these measurements provide support for the volume flow models and this has now been confirmed with intracranial recordings in humans as well (Co-PI Parra). Dr. Parra's pipeline for constructing current-flow models (ROAST) is freely available online. While the models work well at a coarse millimeter scale, our recordings in the macaque show that there is substantial imhomogeneity at the sub-millimeter scale. This is an important focus of ongoing research as it may contribute to substantial intersubject variability found with transcranial current stimulation in humans.

In terms of the second goal (understanding the neural changes) - we published the first study investigating how TCS affects neural activity in the primate brain. The main finding of this study was that 10 Hz alternating currents reduce sensory adaptation. This is an important finding as it shows that other mechanisms (beyond bringing the membrane closer to threshold or entraining a network rhythm) are likely at play in TCS. This work has led to numerous ongoing projects in which we are using this insight to manipulate cognitive performance (e.g. attention , or learning) using alternating currents in human subjects (with NIH support). In a separate set of experiments we found direct evidence that tDCS modulates excitability in primary visual cortex. This effect is relatively long lasting (at least 20 minutes after 20 minutes of stimulation), but quite variable across recording sites. As indicated above, the results of the first aim of this project suggest that this may be caused by inhomogeneities in the intracranial fields- a topic that we contintue to investigate (with NIH Support).

Overall, the ARO support has allowed us to develop novel approaches and techniques to study TCS in the primate brain. The initial findigs have been published but much more work remains to be done. The pilot results that we obtained with ARO support were instrumental in obtaining sustained funding from the NIH BRAIN Initiative to pursue this promising area of research and link it back to future applications in human.

**Training Opportunities:** Several trainees have participated in this project. This ranges from high-school summer interns, undergraduates, graduate students to postdocs. These trainees have learned to work with complex computer models for current flow prediction, obtaining MRI data in macaques, animal surgery, single cell and multi-electrode array electrophysiology, animal behavioral training, and advanced data analysis using Matlab on a high-performance computing cluster. Most of this training was provided in the form of one-on-one work with the mentor.

The graduate students and postdocs also attended several national and international conferences, and seminars on the topic.

**Results Dissemination:** Results of this project have been published in peer-reviewed journals, in conference proceedings, and communicated to many interested listeners at colloquia and invited seminars.

The PI has also given presentations for patient groups, alumni networks, and at schools.

**Honors and Awards:** Nothing to Report

**Protocol Activity Status:**

**Technology Transfer:** Several of our findings contribute to applications of TCS. For instance, by showing that sufficiently large electric fields can be generated in the brain, by identifying novel TCS protocols that can be used in humans (e.g. reduction of adaptation), or by highlighting the potential for factors that contribute to variable outcomes across human subjects.

PI Krekelberg and Co-PI Parra are both actively working with industry to translate some of these findings into practical applications. Several software tools have already been made available on the PI's websites.

**PARTICIPANTS:**

**Participant Type:** PD/PI
**Participant:** Bart Krekelberg
**Person Months Worked:** 3.00 **Funding Support:**
Project Contribution:
International Collaboration:
International Travel:
National Academy Member: N
Other Collaborators:

**Participant Type:** Co PD/PI
**Participant:** Lucas Parra
**Person Months Worked:** 2.00 **Funding Support:**
Project Contribution:
International Collaboration:
International Travel:
National Academy Member: N
Other Collaborators:

**Participant Type:** Postdoctoral (scholar, fellow or other postdoctoral position)
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**Person Months Worked:** 10.00 **Funding Support:**
Project Contribution:
International Collaboration:

International Travel:
National Academy Member: N
Other Collaborators:

**Participant Type:** Technician
**Participant:** Anne McCormick
**Person Months Worked:** 7.00 **Funding Support:**
Project Contribution:
International Collaboration:
International Travel:
National Academy Member: N
Other Collaborators:

**Participant Type:** Graduate Student (research assistant)
**Participant:** Kohitij Kar
**Person Months Worked:** 15.00 **Funding Support:**
Project Contribution:
International Collaboration:
International Travel:
National Academy Member: N
Other Collaborators:

**Participant Type:** Graduate Student (research assistant)
**Participant:** Yinghua Liu
**Person Months Worked:** 15.00 **Funding Support:**
Project Contribution:
International Collaboration:
International Travel:
National Academy Member: N
Other Collaborators:

**Participant Type:** Graduate Student (research assistant)
**Participant:** Yinghua Liu
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International Collaboration:
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National Academy Member: N
Other Collaborators:

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**Title:** Neural Mechanisms of Action of Transcranial Electrical Stimulation
**Authors:** Kohitij Kar
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# RPPR Final Report
as of 24-Jan-2019

**WEBSITES:**

**URL:** https://www.parralab.org/roast/
Date Received:
**Title:** A fully automated, Realistic, vOlumetric Approach to Simulate Transcranial electric stimulation.
**Description:** A fully automated, Realistic, vOlumetric Approach to Simulate Transcranial electric stimulation.
**URL:** https://github.com/klabhub
Date Received:
**Title:** KLabHub - Software sharing
**Description:** Software sharing repository with tools for data analysis and experimental control.

Nothing to report in the uploaded pdf (see accomplishments)