UNDERSTANDING CIRCUIT MECHANISMS OF ELECTROCONVULSIVE THERAPY USING MULTIMODAL MRI

Joan A. Camprodon[1], Tracy Barbour[1], Benjamin Ward[2], Carles Soriano-Mas[3] & Marta Cano[4]

[1]*Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA*
[2]*University of California, Los Angeles, CA, USA*
[3]*Bellvitge Biomedical Research Institute-IDIBELL, Barcelona, Spain*
[4]*Univestitat Autonoma de Barcelona, Barcelona, Spain*

Electroconvulsive therapy (ECT) remains the most effective treatment in psychiatry, and among the most effective in medicine. While our clinical understanding of ECT is significant, it contrasts with how little we know about its neurobiological mechanisms of action. Given how diffuse the induced electric fields are and the fact that ECT leads to a generalized seizure, ECT has been traditionally considered a non-specific neuromodulation treatment. However, neuroimaging research is challenging this notion and suggesting ECT is more focal than previously considered. In this symposium, we will present data from groups working in the Global ECT-MRI Research Collaboration (GEMRIC) using structural and functional MRI to understand predictors and mechanisms of action of ECT at the circuit level.

Dr. Wade will discuss results using functional connectivity MRI to compare the mechanisms of action of ECT to other rapidly acting treatments (serial ketamine infusion and total sleep deprivation), identifying modality-specific mechanisms and treatment-response biomarkers.

Dr. Soriano-Mas will present data from GEMRIC aiming to understand the anatomical antidepressant mechanisms of action of ECT using structural covariance. Changes in structural covariance of the hippocampus and the anterior insula are associated with antidepressant efficacy, highlighting the importance of a circuit-based approach to understanding pathophysiology and the and mechanisms of treatment response.

Dr. Cano will present data from GEMRIC analyzing 148 patients with treatment resistant depression, assessing structural changes (volume, area and thickness) associated with the antisuicidal properties on ECT, and highlighting the role of the anterior cingulate.

Dr. Camprodon will discuss results assessing patterns of functional connectivity that both predict and explain the antisuicidal efficacy of ECT at the circuit level. This study illustrates the use ECT as a systems neuroscience translational tool to identify treatment targets and inform subsequent treatment development research for suicide, using other neuromodulation interventions such as TMS.

* * * * *

POTENTIAL OF ELECTRIC FIELD SIMULATIONS IN CLINICAL PRACTICE

Chris Baeken[1], Martin Tik[2], Oula Puonti[3], Debby Klooster[1], Alex Opitz[4] & Maria Vasileiadi[5]

[1]*Ghent Experimental Psychiatry (GHEP) Lab, Ghent, Belgium*
[2]*Brain Stimulation Lab, Psychiatry and Behavioral Sciences, Stanford, CA, USA*
[3]*Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital Amager and Hvidovre, Copenhagen, Denmark*
[4]*University of Minnesota, Minneapolis, MN, USA*
[5]*Medical University of Vienna, Vienna, Austria*

Brain stimulation induced electric field simulations can identify how brain regions are affected depending on the individual's gyral folding pattern. The information about the distribution and strength of the electric fields can be used to derive personalized stimulation parameters or be considered retrospectively in statistical analyses. In this symposium,

First, Oula Puonti (Danish Research Center for Magnetic Resonance) will give an introduction on electric field simulations in practice. Furthermore, he will talk about the link between field modeling and personalized stimulation protocols and present results on the validation of the simulations using invasive and non-invasive approaches identifying crucial aspects for accurate electric field estimates.

Debby Klooster (Ghent University) will demonstrate how electric field simulations could be used in clinical practice to derive the optimal coil position. Current clinical routines assume highest stimulation effects under the center of the coil. This model falls short in explaining the real induced currents. Using data from the HCP, she shows the added value of electric field simulations over simple projection methods.

Alexander Opitz (University of Minnesota) will talk about combining electric field modeling with traditional meta-analysis to simulate effects of tDCS. Due to differences in electrode montages and stimulation intensities across studies, results are difficult to aggregate for meta-analytic inferences. A novel meta-analytic method relating behavioral effect sizes to electric field strength was developed to identify brain regions underlying the largest tDCS-induced working-memory improvement.

Maria Vasileiadi (Medical University Vienna) will talk about the application of electric field simulations in pre-surgical language mapping. TMS mapping has been shown to be clinically useful and safe but standard approaches are lacking the accuracy of direct cortical stimulation. She will propose a procedure including fMRI, causal mapping using TMS and improved estimation of effective stimulation targets by combining electric field modeling with high-precision neuronavigation.

INTRODUCTION TO ELECTRIC FIELD MODELING: HOW, WHY, AND WHAT IS STILL MISSING?

Oula Puonti

Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital Amager and Hvidovre, Copenhagen, Denmark

The electric field induced in the brain by non-invasive brain stimulation approaches, such as transcranial magnetic or electric stimulation (TMS/TES), often has a complex spatial distribution shaped by the individual anatomy of a subject (Saturnino et al. 2019, Puonti et al. 2020). Using electric field simulations we can study the magnitude and direction of the induced field in the brain and link its properties to stimulation outcomes, or to plan the stimulation protocol so that the direction and magnitude of the field in a given target is matched for all subjects in a study. In this talk, I will give a basic introduction to electric field modeling: how the simulations are done in practice, why they are useful, and what we are currently still missing. I will cover the different steps in a simulation pipeline, starting from an MRI scan all the way to the electric field estimates, and how the output from such pipeline should be interpreted. To demonstrate how simulations can be exploited, I will present specific examples of how to analyze data that has already been acquired and how to use the simulations in the planning of new studies. In relation to prospective planning, I will also talk about the link between field modeling and personalized stimulation protocols. I will then present results on the validation of the simulations using invasive and non-invasive approaches, and discuss which aspects of the modeling are most crucial for getting accurate electric field estimates. Finally, I will conclude with an outlook for the future developments that are needed to fill the gap between simulation and stimulation.

References:

1. *Saturnino GB, Puonti O, Nielsen JD, Antonenko D, Madsen KH, Thielscher A: SimNIBS 2.1: a comprehensive pipeline for individualized electric field modelling for transcranial brain stimulation. Brain and human body modeling 2019; 3-25*
2. *Puonti O, Van Leemput K, Saturnino GB, Siebner HR, Madsen KH, Thielscher A: Accurate and robust whole-head segmentation from magnetic resonance images for individualized head modeling. NeuroImage. 2020; 219:117044*

DO ELECTRIC FIELD SIMULATIONS HAVE ADDED VALUE FOR DETERMINATING TMS COIL POSITIONS AT THE SCALP FOR OPTIMAL TARGETING?

Debby C.W. Klooster[1,2], G. Vanhollebeke[1] & Chris Baeken[1,2]

[1]Ghent Experimental Psychiatry Laboratory, Ghent University, Ghent, Belgium
[2]Department of Electrical Engineering, Eindhoven University of Technology, Eindhoven, the Netherlands

Transcranial magnetic stimulation has shown promising results in treatment of depression. Personalized stimulation parameters to improve the clinical efficacy of stimulation is a hot topic. Personalized cortical stimulation targets have been proposed, for example based on the functional connections with the deeper subgenual anterior cingulate cortex. In clinical practice, the coil position is a simple projection above this predefined cortical stimulation target. However, individual gyral folding patterns shape the distribution of the TMS induced electric fields within the brain and hence the projection method might not be optimal to determine the coil position. In line, it has been suggested that electric field simulations can provide added value in determination of the ideal TMS coil position at the scalp (Klooster et al. 2021). However, this has not been investigated in detail.