

management, and present initial findings from recently completed and ongoing clinical trials.

#### Abstract

When COVID-19 first emerged, many researchers were focused on its impact on the lungs. As we have learned more about SARS-CoV-2 and resulting COVID-19, we have discovered that patients present a greater complexity in the context of the neurotrauma and the pulmonary lesions can become an aggravation of the neuroinvasion of the coronavirus and originate from cerebral injury. Recently, it has been suggested that noninvasive brain stimulation could be a valuable tool for the management of the early and postacute phase of patients with COVID-19. This session will present the results of our investigation of the High-definition transcranial direct current stimulation effects during the acute and chronic recovery phase from COVID-19. The prognostic factors and clinical predictors that contribute to greater response to treatment will be presented and directions for future research will be discussed.

#### Research Category and Technology and Methods

**Clinical Research:** 9. Transcranial Direct Current Stimulation (tDCS)

**Keywords:** HD-tDCS, Coronavirus disease, Noninvasive brain stimulation, Long COVID-19

<http://dx.doi.org/10.1016/j.brs.2023.01.230>

Abstract key: PL- Plenary talks; S- Regular symposia oral; FS- Fast-Track symposia oral; OS- On-demand symposia oral; P- Posters

#### OS07.2

### POTENTIAL APPLICATION OF TRANSCRANIAL ELECTRICAL STIMULATION (TES) TECHNIQUES IN THE CONTEXT OF COVID-19 CLINICAL COURSE: FROM THEORY TO REAL-WORLD APPLICATION

Giuseppina Pilloni<sup>1</sup>, Leigh Charvet<sup>1</sup>, Abhishek Datta<sup>2</sup>, Marom Bikson<sup>3</sup>. <sup>1</sup>NYU Grossman School of Medicine, USA; <sup>2</sup>Soterix Medical Inc., USA; <sup>3</sup>City College of New York, USA

#### Abstract

The novel SARS-CoV-2 virus has infected millions of people around the world, and will become endemic, resulting in an urgent need to discover and validate inexpensive and accessible treatments that can reduce morbidity and persistent post-infectious symptoms. Noninvasive brain stimulation methods, such as transcranial electrical stimulation (tES), may have a potential role in the treatment of Coronavirus Disease 2019 (COVID-19) related symptoms. This potential is theorized based on the known mechanisms of biological action and demonstrated benefits in non-COVID-19 patients for various known sequelae of COVID-19 illness and recovery (e.g., fatigue, cognitive dysfunction, central sensitization, and emotional dysregulation), with now several initiatives of its application in the context of COVID-19 clinical course. Here, we will summarize the technological advantages, the rationale, and mechanism of action of using tES techniques to manage COVID-19 infection through four pathways: (1) Acute intervention, (2) Add-on treatment to augment rehabilitation following critical illness, (3) Post-Acute Sequelae of SARS-CoV-2, and (4) Treatment of outbreak related mental distress exacerbated by surrounding psychosocial stressors related to COVID-19 pandemic.

#### Research Category and Technology and Methods

**Clinical Research:** 9. Transcranial Direct Current Stimulation (tDCS)

**Keywords:** tES, PASC, SARS-CoV-2 Infection

<http://dx.doi.org/10.1016/j.brs.2023.01.231>

Abstract key: PL- Plenary talks; S- Regular symposia oral; FS- Fast-Track symposia oral; OS- On-demand symposia oral; P- Posters

#### OS07.3

### EFFICACY OF TRANSCRANIAL DIRECT CURRENT STIMULATION AND COGNITIVE TRAINING FOR THE NEUROCOGNITIVE SYMPTOMS OF LONG COVID-19

Andre R. Brunoni, Beatriz Cavendish, Bianca Silva Pinto, Rebeca Pelosof, Juliana Pereira, Adriano Neto, Kallene Vidal. *University of São Paulo Medical School, Brazil*

#### Abstract

COVID-19 has been associated with cognitive dysfunction and psychiatric disorders. The subjective cognitive complaints can occur in approximately 90% of these individuals after the infection by COVID-19. In this context, there is an urgent need to develop treatment for Post-Acute Sequelae of Sars-Cov2 (PASC). The transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation intervention with potential as a PASC treatment as it can modulate neuronal excitability, brain vascular function, which can result in modulation of neural circuits cognitive, and psychiatric disorders. Preliminary results from a pilot study a decrease of cognitive and emotional complaints evaluated by A-PASC inventory. The neuropsychological assessment showed that the participants had a better performance for delayed and immediate recall in the verbal episodic memory task. They showed an improving trend in lexicon assess, and in phonemic verbal fluency. The same was observed for the sustained attention task. Also, the participants showed a trend in becoming faster and more accurate in processing speed, and in executive function (inhibitory control, cognitive flexibility and time management). Based on these findings, we are performing a pilot randomized sham-controlled trial consisting of 20-minute, 2mA, 20 daily sessions of bilateral prefrontal (anodal-left/cathodal-right) tDCS (1x1 Mini-CT, Soterix Medical, New York, NY) plus online cognitive training using the BrainHQ platform (Posit Science, San Francisco, Glenn Smith). We will compare the efficacy of active vs. sham tDCS, combined with cognitive training, to improve these neurocognitive symptoms.

#### Research Category and Technology and Methods

**Translational Research:** 9. Transcranial Direct Current Stimulation (tDCS)

**Keywords:** tDCS, Long COVID-19, Neurocognitive Symptoms

<http://dx.doi.org/10.1016/j.brs.2023.01.232>

Abstract key: PL- Plenary talks; S- Regular symposia oral; FS- Fast-Track symposia oral; OS- On-demand symposia oral; P- Posters

#### OS07.4

### TDCS AS TELEHEALTH INTERVENTION TO REACH PATIENTS WITH POST-ACUTE SEQUELAE OF SARS-COV-2 (PASC)

Leigh Charvet<sup>1</sup>, Giuseppina Pilloni<sup>1</sup>, Allan George<sup>1</sup>, Tehila Eilam-Stock<sup>2</sup>, Matthew Lustberg<sup>1</sup>, Abhishek Datta<sup>3</sup>, Marom Bikson<sup>4</sup>. <sup>1</sup>NYU Grossman School of Medicine, USA; <sup>2</sup>Burke Rehabilitation Hospital, USA; <sup>3</sup>Soterix Medical Inc., USA; <sup>4</sup>City College of New York, USA

#### Abstract

There is a critical need for therapeutic interventions for Post-Acute Sequelae (PASC) of SARS-CoV-2 infection patients worldwide. tDCS has the potential for therapeutic targeting of these PASC symptoms, with devices that can be portable and wearable for home-based access. At-home tDCS access is highly relevant to complete the necessary clinical trials for PASC and has the potential to provide patients with an immediate treatment option. We have led the field in rigorous, reliable, and standardized home-based brain stimulation with the development of the remotely supervised or RS-tDCS platform. Participants are provided with remotely-controlled devices, trained in safe and effective operation, and then supervised for daily use through live videoconference. Extensively tested over >8 years (>12,000 at-home tDCS sessions in >500 patients to date), the feasibility of our RS-tDCS procedures has been verified for use across all ages (18-80 years), including those with advanced cognitive or motor disabilities and/or limited technical experience, and also reaching those at socioeconomic healthcare disadvantage for inclusion in RCTs. The RS-tDCS platform has allowed for the continued enrollment in ongoing RCTs during the COVID-19 onsite clinical research pause (with >100 participants by completing all study procedures from home). The telehealth delivery of the intervention results in rapid enrollment and high retention and adherence for repeated and extended sessions (e.g., >97% completion rates across RCTs to date). While tDCS remains under investigational status in the U.S., in 2019, we also launched tDCS as a clinical telehealth service as innovative care. In this at-home service, tDCS is delivered to patients at home and stimulation parameters can be individualized to be paired with interventions such as physical exercise, online adaptive computerized cognitive training, and guided mindfulness meditation. Patients with PASC, seen through our tDCS program, will be presented as examples of the at-home tDCS treatment approach.

**Research Category and Technology and Methods****Clinical Research:** 9. Transcranial Direct Current Stimulation (tDCS)**Keywords:** tDCS, Telehealth Intervention, PASC, SARS-CoV-2<http://dx.doi.org/10.1016/j.brs.2023.01.233>

Abstract key: PL- Plenary talks; S- Regular symposia oral; FS- Fast-Track symposia oral; OS- On-demand symposia oral; P- Posters

**OS08.1****COMBINED TMS-EEG-fMRI TO UNRAVEL PHASE SENSITIVITY OF BOLD RESPONSE**Mark S. George<sup>1</sup>, Truman Brown<sup>1</sup>, Paul Sajda<sup>2</sup>. <sup>1</sup>MUSC, USA; <sup>2</sup>Columbia University, New York, NY, USA**Symposium title:** Travelling and optimizing parameter space for interleaved TMS/fMRI applications**Symposium description:** Interleaved TMS/fMRI has a huge potential to provide valuable insights into TMS' mechanisms-of-action on a neural level. This increase of knowledge has led to important improvements of TMS applications in clinical routine and basic research. Nonetheless, the application of interleaved TMS/fMRI bears a number of challenges itself that result in variable outcomes. These include: subject motion, influence of peripheral effects on BOLD response and the poorly understood relationship between BOLD response and neurophysiological effects due to TMS. It is the aim of this symposium to address a variety of these open questions via the application of state-of-the-science technical advancements. First, we will discuss the application of combined TMS-EEG-fMRI investigating the relationship between phase sensitivity and BOLD-response during stimulation. Then, we will evaluate how different brain areas show varying dose-response-patterns based on BOLD increase during TMS. Next, we will show how advanced online motion tracking can account for subject movement via real-time dose adjustments. Finally, we will discuss the influence of peripheral effects (somatosensory, acoustic) in the context of interleaved TMS/fMRI applications. Our speakers will discuss here different technical advancements, which progress the application of interleaved TMS/fMRI and provide new insights into its mechanisms-of-action. Talk 1: Mark S. George Combined TMS-EEG-fMRI to unravel phase sensitivity of BOLD response Talk 2: Martin Tik Whole brain TMS-evoked dose-response patterns of BOLD signal Talk 3: Christian Windischberger Real-time motion tracking for online dose adjustments Talk 4: Anna-Lisa Schuler Potential influence of peripheral effects during interleaved TMS/fMRI**Abstract**

Our group at MUSC has succeeded in creating a system capable of combining TMS, fMRI and EEG. In this talk we will describe this system in both its original and newer modifications. We will then review studies over the prefrontal cortex demonstrating how local and distant TMS induced BOLD responses correlate with different EEG phase at the prefrontal region where TMS was applied.

**Research Category and Technology and Methods****Translational Research:** 10. Transcranial Magnetic Stimulation (TMS)**Keywords:** TMS, fMRI, EEG<http://dx.doi.org/10.1016/j.brs.2023.01.234>

Abstract key: PL- Plenary talks; S- Regular symposia oral; FS- Fast-Track symposia oral; OS- On-demand symposia oral; P- Posters

**OS08.2****WHOLE BRAIN TMS-EVOKED DOSE-RESPONSE PATTERNS OF BOLD SIGNAL**Martin Tik<sup>1</sup>, Michael Woletz<sup>2</sup>, Maria Vasileiadi<sup>2</sup>, David Linhardt<sup>2</sup>, Anna-Lisa Schuler<sup>2</sup>, Nolan Williams<sup>1</sup>, Christian Windischberger<sup>2</sup>. <sup>1</sup>Stanford University, USA; <sup>2</sup>Medical University of Vienna, Austria**Abstract**

New developments in interleaved TMS/fMRI provide new possibilities in understanding TMS' mechanisms-of-action. In particular, combining TMS with fMRI offers the unique opportunity to investigate dose-response

relationships of stimulation in brain areas beyond the primary motor cortex. Using setups with optimized signal-to-noise ratio, it is not only possible to evaluate dose-response-patterns at the stimulation target area but also on a whole brain network level.

In this talk we will discuss advantages of dose-response mapping for the understanding of TMS' mechanisms-of-action and their potential for clinical applications using high-sensitivity interleaved TMS/fMRI. In this respect, we will evaluate dose-response patterns at the motor cortex and then go beyond by investigating these relationships in DLPFC stimulation. This talk will provide valuable insights into new opportunities to better understand the influence of TMS on cortical excitability and brain network modulations.

**Research Category and Technology and Methods****Basic Research:** 10. Transcranial Magnetic Stimulation (TMS)**Keywords:** Interleaved TMS/fMRI, dose-response, DLPFC<http://dx.doi.org/10.1016/j.brs.2023.01.235>

Abstract key: PL- Plenary talks; S- Regular symposia oral; FS- Fast-Track symposia oral; OS- On-demand symposia oral; P- Posters

**OS08.3****NEURONAVIGATION-BASED IMPROVEMENTS OF CONCURRENT TMS/fMRI STUDIES**Christian Windischberger<sup>1</sup>, Michael Woletz<sup>1</sup>, Sarah Grosshagauer<sup>1</sup>, Maria Vasileiadi<sup>1</sup>, Martin Tik<sup>2</sup>. <sup>1</sup>Medical University of Vienna, Austria; <sup>2</sup>Stanford University, USA**Abstract**

The concurrent combination of transcranial magnetic stimulation and functional magnetic resonance imaging is one of the most challenging setups in the field of non-invasive brain stimulation as the Lorentz forces from administering high-intensity TMS pulses in the strong magnetic field of the MR scanner cause considerable mechanical stress on the hardware involved and requires robust device mounting setups. In addition, TMS coil position over the defined cortical targets must be constant in order to achieve robust stimulation results. Even small changes in coil-cortex distance of a few millimetres will vary stimulation intensity by 10% MSO. Successful concurrent TMS/fMRI thus requires an approach balancing motion restraining and subject comfort. Neuronavigation inside the MR scanner bore can be extremely helpful for accurate tracking of subject and stimulation coil. Here we will show how position information can be used to improve concurrent TMS/fMRI outcomes. The most straightforward way of using position information would be for quality control purposes, i.e. to repeat motion-affected runs or exclude subjects with high motion behaviour. Neuronavigation data can also be used as feedback to subjects in order to allow them to regain and stabilize an intended head position throughout the concurrent TMS/fMRI scan. Finally, positioning information during scanners can also yield accurate coil-cortex measurements that serve as a modulator of stimulation intensity. Such, it is possible to achieve constant stimulation amplitudes at the target site even in cases where subjects increase their distance to the stimulation coil.

**Research Category and Technology and Methods****Basic Research:** 10. Transcranial Magnetic Stimulation (TMS)**Keywords:** TMS/fMRI, Neuronavigation, motion<http://dx.doi.org/10.1016/j.brs.2023.01.236>

Abstract key: PL- Plenary talks; S- Regular symposia oral; FS- Fast-Track symposia oral; OS- On-demand symposia oral; P- Posters

**OS08.4****POTENTIAL INFLUENCE OF PERIPHERAL EFFECTS DURING INTERLEAVED TMS/fMRI**Anna-Lisa Schuler<sup>1</sup>, Martin Tik<sup>2</sup>, Giovanni Pellegrino<sup>1</sup>. <sup>1</sup>IRCCS San Camillo Hospital, Venice, Italy; <sup>2</sup>Stanford University, USA**Abstract**

The combination of TMS with fMRI has the potential to unravel specific effects of TMS including evaluation of excitability patterns and whole brain