To better understand the physiology of the indirect effects of tDCS, we investigated the raphe activity in response to acute and chronic prefrontal-tDCS, in particular by analysing serotonin (5-HT) neural activity by single-unit in-vivo electrophysiology and HPLC. Indeed, one of the main neurotransmitters involved in the pathophysiology and psychopharmacology of depression is 5-HT, released by neurons of the dorsal raphe nuclei. We observed different spontaneous firing outcomes after acute and chronic tDCS, with some effects lasting up to one month. Additionally, in the motor cortex, we observed that the combination of tDCS and physical activity results in a boosting effect of neural plasticity in both hemispheres.
Altogether, these data indicate a strong functional influence of tDCS on cortical connectivity, and not only in the directly stimulated region.

Research Category and Technology and Methods
Basic Research: 9. Transcranial Direct Current Stimulation (tDCS)
Keywords: Serotonin, Depression, Motor cortex, Dendritic spines

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

OS06.3

COMBINING GAMMA TACS STIMULATION WITH ROBOTIC REHABILITATION AFTER STROKE IN MICE: THE ROLE OF PARVALBUMIN INTERNEURONS

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Abstract
Functional deficits after stroke in motor cortex represent a main cause of disability worldwide. Physical therapy alone, even if guided by robotic devices, is often uneffective and it is widely accepted that it should be coupled with neuromodulatory strategies to promote “activity-dependent plasticity” in the spared tissue. These strategies can involve Non-Invasive Brain Stimulation (NIBS) techniques and among them, transcranial Alternating Current Stimulation (tACS) that is able to synchronize neural activity in a defined area and frequency. In humans Gamma frequency reduction has been reported after stroke and associated to worse hand functionality. Moreover, functional studies has related Gamma genesis with the synchronous discharge of Parvalbumin Interneurons (PV-IN). Unfortunately, a clear roadmap for rehabilitation involving these new strategies is missing and the neurophysiological mechanisms underlying their effects on functional damage are still poorly defined.
Here, we used a mouse model of ischemic injury to investigate the effect of ischemic stroke in motor cortex on Gamma band motor-related synchronization and PV-IN activity in spared premotor cortex. We also tested novel rehabilitative approaches by combining robotic rehabilitation with Gamma band stimulation using both optogenetic stimulation of PV-IN and a more translational non-invasive 40 Hz tACS.
By means of electrophysiological recordings and wide-field imaging in awake behaving mice we found that stroke significantly decreases Gamma band power in perilesional healthy tissue and impairs PV-IN activity in perilesional and contralesional hemisphere, despite PV-IN movement-related activity still persists in premotor cortex. We demonstrated that a specific optogenetic 40Hz stimulation in spared premotor cortex combined with robotic rehabilitation successfully restored motor function after stroke. Moreover, the same results were obtained using a 40Hz tACS stimulation combined with robotic rehabilitation which also increased PV-IN connections in perilesional premotor cortex.
These results pave the way for novel highly successful and tolerated rehabilitative approaches in post-stroke clinical therapy.

Research Category and Technology and Methods
Basic Research: 8. Transcranial Alternating Current Stimulation (tACS)
Keywords: Gamma band, Robotic rehabilitation, Parvalbumin Interneurons, stroke

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OS06.4

NEUROPLASTICITY AND EEG CONNECTIVITY, HOW TO MEASURE AND TO USE AS POTENTIAL BIOMARKERS IN NEURO-REHABILITATION TREATMENT

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Abstract
Behavior and cognition are characterized by engagement of functional distributed networks within the brain. Such networks organization is especially significant in pathological condition modulating brain activity such as stroke, and requires a high degree of intra-modal and inter-modal integration of information flow arriving from several, different and often remote brain sources. These networks dynamically connect adjacent and/or remote cortical neuronal assemblies via cortico-cortical connections. These neural networks undergo relevant changes due to stroke insult. Currently, non-invasive brain stimulation (NIBS) techniques, such as transcranial electrical stimulation (tES), as already illustrated in the previous talks of this symposium, are adopted to modulate stroke effect on the brain, acting on networks proprieties and connectivity. Novel approach, also applying concepts from graph theory to neurophysiological data, is a promising new way to characterize brain activity, providing a method to evaluate whether functional connectivity patterns between brain areas resemble the organization of theoretically efficient, flexible or robust networks, based on strength of synchronization of different brain regions. Here, we will summarize the possible aspect of analyzing connectivity changes due to NIBS in stroke mouse model, and how to apply EEG graph theory analyses on stroke patients in order to predict functional recovery basing of classification procedures. More specifically, in the mouse model, an increased total functional coupling following tDCS might correlate with the speed rather than the degree of recovery, while Small World index in the acute stroke patient, gives a significant weight of recovery prediction.

Research Category and Technology and Methods
Translational Research: 9. Transcranial Direct Current Stimulation (tDCS)
Keywords: tDCS, EEG, Functional coupling, stroke

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

OS07.1

HD-TDCS IN ACUTE AND LONG-TERM COVID-19

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Symposium title: The potential role of tDCS in the management of Post-Acute Sequelae of SARS-COV-2 (PASC)
Symposium description: The novel SARS-CoV-2 virus has infected millions of people worldwide. Post-infectious symptoms, referred to as Post-Acute Sequelae of SARS-CoV-2 (PASC), affect a large and growing segment of survivors, lasting months or even years without recovery. With continuous COVID-19 infections, PASC is a growing problem for public health. Therefore, effective and accessible treatment options need to be evaluated urgently. PASC symptoms are multi-systemic and can vary by the individual in clinical presentation, and its underlying pathological mechanisms remain uncharacterized. tDCS is a well-tolerated and extensively characterized noninvasive neuromodulation technique, and is effective in targeting the neuropsychiatric symptoms that define PASC (i.e., fatigue, cognitive, pain, emotional) including in other post-viral conditions. In addition, tDCS may have a larger role in the management of persisting respiratory symptoms. We will provide an overview of the theoretical basis and work to date supporting tDCS as a tool for PASC

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

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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

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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

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OS07.3

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

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Abstract
COVID-19 has been associated with cognitive dysfunction and psychiatric disorders. The subjective cognitive complaints can occurred 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 perform 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 an 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

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OS07.4

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

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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.