AI in Neurorehab: Machine Learning Informs Real-Time Delivery of Non-Invasive Brain Stimulation for Poststroke Motor Recovery

After carefully stretching a cap full of electroencephalography (EEG) electrodes over a participant's head, Dr. Sara Hussain checked that each computer that was needed to carry out her experiment – four in total – was operating properly. As a postdoctoral fellow at the Human Cortical Physiology and Neurorehabilitation Section within the National Institute of Neurological Disorders and Stroke (NINDS), she was excited to be working on a new study looking at the relationships between a specific pattern of EEG signals recorded over the sensorimotor cortex (called mu rhythms), the excitability of corticospinal tract neurons, and motor learning in adults without brain injury.

The corticospinal tract carries the majority of outgoing voluntary upper extremity motor commands, and Dr. Hussain and her postdoctoral mentor predicted that delivering transcranial magnetic stimulation (TMS) to the corticospinal tract during specific sensorimotor mu rhythm phases would alter motor learning. To answer this question, Dr. Hussain performed a technically demanding study that involved analyzing human EEG signals in real time and delivering stimulation during these key mu rhythm phases. After months of data collection (including many late-night sessions), Dr. Hussain discovered that they were right.

Dr. Hussain's postdoctoral research projects continued to gain momentum as she also began the arduous task of interviewing for faculty positions. While preparing manuscripts for submission and wondering where she might be living the following year, she continued work on a similar study, this time in stroke survivors – until March of 2020. The COVID pandemic halted her data collection with human participants, and the lab closed for several months. While working remotely, Dr. Hussain continued analyzing her data and began negotiations for her new position at the University of Texas at Austin. She even made a last minute trip to Austin to find a home before travel restrictions set in. Dr. Hussain kept moving her line of research forward and began thinking about the projects she would conduct in her new lab, which she officially opened in January of 2021. Given her transition to a faculty position and the timing of the COVID pandemic, she unfortunately was not able to complete her study in stroke survivors during her postdoc.

While the pandemic was a major barrier to productivity in many ways, it also provided Dr. Hussain with some unexpected opportunities – namely, more time to think about the future of her research projects and learn new skills. She had been exposed to machine learning techniques during her postdoctoral training, but she never had the chance to try them herself.

Dr. Hussain's first semester as an Assistant Professor involved teaching remotely and ordering equipment for her new laboratory. However, she also decided this was the perfect moment to test out how machine learning could be leveraged to optimize the effects of TMS using an existing dataset. Machine learning is an artificial intelligence (AI) application that uses mathematical models of data to help a computer learn without explicit instruction. In this case, Dr. Hussain's goal was to develop data-driven approaches that could identify EEG activity patterns that are most favorable for enhancing motor function using TMS.

Dr. Hussain and one of her former colleagues from her postdoctoral lab began working to develop a personalized machine learning framework that could identify EEG activity patterns (which she also refers to as "brain states") that predict when TMS best activates the corticospinal tract. In 2022, they published this approach, which applies linear discriminant analysis to whole-brain EEG signals that have been converted into the frequency domain. In this context, linear discriminant analysis is a supervised machine learning technique that uses labeled data to identify EEG patterns that predict when single-pulse TMS elicits large or small muscle twitches. After developing her approach, Dr. Hussain began creating a customized analysis system that could identify these EEG patterns in real time so that TMS could be triggered to occur during the EEG patterns of interest. Next, one of her PhD students started testing this real-time machine learning-driven approach in adults without brain injuries and soon obtained promising results. Then, Dr. Hussain and her lab members began testing this technique in participants who had experienced a stroke that affected their motor function.

One of the major challenges in developing therapeutic strategies for stroke rehabilitation is that each stroke survivor has a different lesion size, shape, and location, and many poststroke brain stimulation approaches don't account for these differences. However, Dr. Hussain's machine learning approach is unique in that it is fully personalized, so it is not negatively affected by this variability between people. Another major strength of her approach is that the EEG data are processed and analyzed in real time to immediately inform the delivery of TMS. Although currently Dr. Hussain and her team are in the "proof-of-concept" stage of this work, she anticipates using this approach to deliver therapeutic brain stimulation interventions capable of improving poststroke hand function in the future.

The preliminary data collected by Dr. Hussain and her laboratory helped drive her first grant applications as an independent investigator. In March and July 2024, she was thrilled to receive the news that her NINDS R21 and NICHD-NCMRR Early Career R03 grants for this overall line of work were officially funded. These grants aim to establish the methodological framework and mechanistic rationale for future personalized, machine learning-driven brain state-dependent TMS interventions in stroke survivors, while also identifying clinical inclusion criteria for large-scale poststroke studies that use this technique.

Data collection for Dr. Hussain's new grants has begun, and results from their first few sessions in stroke survivors are encouraging. However, she is aware that this line of work is in its infancy, and that her technique can still be significantly improved. Looking to the future, Dr. Hussain hopes to further optimize her lab's current machine learning-driven EEG-TMS approach for people who have experienced a stroke, and eventually, combine it with targeted motor training to enhance poststroke motor recovery.

The machine learning platform developed by Dr. Hussain is a novel approach that could be used in the future to promote recovery of motor function in people with stroke. It also represents an important example of how neurorehabilitation researchers can leverage artificial intelligence techniques to identify relevant brain activity patterns to enhance the effects of rehabilitation, and ultimately, improve outcomes for patients.

As for Dr. Hussain? She never expected to be doing this kind of research. “Growing up, math, science, programming… these were not things that I believed were ‘for me.’ The biggest lesson I’ve learned in diving into machine learning is that if you really do want to learn something new and you fully commit yourself to the process of learning it – you can. Never let anyone tell you otherwise.”