Predictive biomarkers of stroke recovery based on electrophysiological readouts

Susanne Dyck, PhD student

Home Program: International Graduate School of Neuroscience, Ruhr-University Bochum, Germany
Home Supervisor: Prof. Dr. Christian Klaes
Host Lab: Hummel Lab, Brain Mind Institute, EPFL, Switzerland
Host Supervisor: Prof. Dr. Friedhelm Hummel & Dr. Sylvain Harquel
Stay Duration: 01.08.2022 - 21.10.2022

With the support of the **NENS exchange grant**, I joined the Hummel lab from 1.08.2022 to 21.10.2022 at the Biotech Campus in Geneva, Switzerland, where I worked on the project “Predictive biomarkers of stroke recovery based on electrophysiological readouts”.

Despite considerable improvements in treatment and rehabilitation measures, stroke is one of the leading causes for long-term disability (Smajlovic, 2015). The cognitive and motor impairments caused by stroke can put a strain on the individual’s quality of life and on our healthcare system. While some patients naturally recover, others do not respond even to advanced therapies. To possibly explain, and ultimately predict, the very heterogeneous recovery outcomes, it is necessary to unravel the neural mechanisms underlying motor recovery. This would also pave the way to optimized therapeutic strategies tailored to the individual.

The TiMeS (“Towards Individualized Medicine in Stroke”) project is a longitudinal study where a large cohort of stroke-patients is evaluated in a multi-modal manner via neuroimaging recordings and behavioral assessments at various stages of stroke chronification. The study is realized in close collaboration with local clinics and aims at greatly contributing to the research field of stroke rehabilitation.

I worked on a subset of the TiMeS dataset, namely the resting-state EEG data of the acute stroke stage. The project goal of my internship was to build an analysis pipeline and a database for the functional connectivity analysis of the resting-state EEG data using Brainstorm (Tadel et al., 2011). Another aim was to use the database to investigate resting-state functional connectivity changes in stroke patients compared to healthy elderly controls.

In the first step, I preprocessed the resting-state EEG data with Matlab and Fieldtrip by using a preprocessing script from Dr. Sylvain Harquel. In total, I preprocessed the data of 48 stroke patients and 18 healthy elderly controls. Then, I imported the clean resting-state EEG data into a Brainstorm database. With the help and supervision of Dr. Sylvain Harquel, we developed an analysis pipeline for resting-state EEG functional connectivity at the source level. The pipeline is partially based on the recent work by Snyder et al. (2021) and translated into Brainstorm. The analysis pipeline and the individual steps are illustrated and explained in Figure 1. In the end, a connectivity matrix with the dimensions 62x62x6 (since 62 regions of interests (ROIs) and 6 frequency bands have been used) is obtained for each individual subject. During my internship, I managed to include 24 subjects in the patient database and 16 subjects in the healthy elderly control database. The final connectivity matrices of these subjects have been imported into a shared database to perform a group comparison. We used a thresholding based on sparsity to transform the weighted connectivity matrices to binarized versions for further analysis. A preliminary group contrast between patients and controls suggests stronger connections in lower frequency bands (delta and theta) and weaker connections in alpha and beta frequency bands in the stroke patient group compared to the healthy elderly controls. While these results are preliminary and only the effect in the lower beta band survives a correction for multiple comparisons, they are in line with previous studies that showed lower connectivity measures in stroke patients compared to controls in the alpha and beta band (Van Kaam et al., 2018). To quantify the organization of the functional connectivity networks in the stroke and the control group, we explored a graph-theory based approach where the network organization is described in terms of segregation and integration. Important metrics in this regard are the modularity (the community structure of a network) and the global efficiency (how well information is transferred or how direct the communication in a network is). To compute these graph-theoretical measures, we used the Brain Connectivity Toolbox (Rubinov & Sporns, 2010) for Matlab. Our preliminary analysis suggests a reduced global efficiency in the functional connectivity network of the stroke patient group compared to the control group. Left for future work, the database needs to be expanded by including more stroke patients. Furthermore, the functional connectivity and graph-theory measures will be correlated to behavioral performance measures to extract possible electrophysiological readouts as markers for motor recovery in stroke patients.

To conclude, the skills I have acquired during my research stay in the Hummel Lab will be of great benefit for the final project within my PhD studies, where I will perform functional connectivity analysis of EEG data as well.

I would like to thank Prof. Dr. Friedhelm Hummel and Dr. Sylvain Harquel for their expertise, supervision and scientific input. I would also like to thank all members of the Hummel Lab for many fruitful discussions and the wonderful time in Geneva.

Finally, I want to express my great appreciation and gratitude for receiving the NENS exchange grant which made this experience possible in the first place.

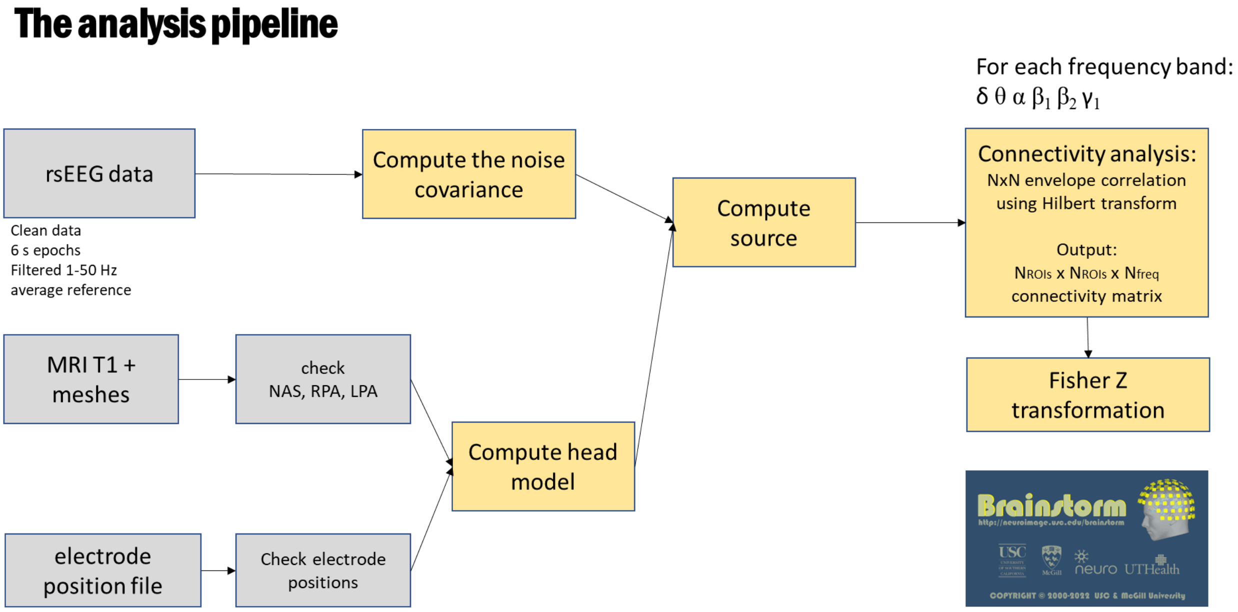

Figure 1: The analysis pipeline for functional connectivity analysis at the source level using Brainstorm. The input consisted of the resting-state EEG (rsEEG) data, the anatomical MRI T1 scans and meshes, where the anatomical landmarks such as Nasion (NAS), right ear (RPA) and left ear (LPA) have been manually checked, and the electrode position file, where the positions have been visually checked and corrected if needed. Based on the anatomical and the electrode position files, a head model has been computed. Together with the noise covariance, calculated from the resting-state EEG recordings, a source model has been computed. For dimensionality reduction, we used an anatomical atlas (Mindboggle atlas, provided by Brainstorm), that consisted of 62 regions of interests (ROIs). Finally, an NxN envelope correlation using Hilbert transform has been computed on the level of ROIs for 6 frequency bands (delta: 1-4Hz; theta: 5-7Hz; alpha: 8-12Hz; beta1: 14-20Hz; beta2: 21-30Hz; gamma1: 30-40Hz). The final output is a connectivity matrix with the dimension 62x62x6, since 62 ROIs have been used and 6 frequency bands have been specified. Lastly, we performed a Fisher-Z-transformation on the obtained connectivity matrices which is recommended for further statistical analysis. While the steps in the gray boxes have to be performed manually, the steps in the yellow boxes are automated in a Matlab script.

References:

Rubinov, M., & Sporns, O. (2010). Complex network measures of brain connectivity: uses and interpretations. *Neuroimage, 52(3), 1059-1069.*

Smajlovic, D. (2015). Strokes in young adults: epidemiology and prevention. *Vasc Health Risk Manag 11:157–64*

Snyder, D. B., Schmit, B. D., Hyngstrom, A. S., & Beardsley, S. A. (2021). Electroencephalography resting‐state networks in people with Stroke. *Brain and behavior*, *11*(5), e02097.

Tadel, F., Baillet, S., Mosher, J. C., Pantazis, D., Leahy, R. M. (2011). Brainstorm: A User-Friendly Application for MEG/EEG Analysis*. Computational Intelligence and Neuroscience, vol. 2011, ID 879716*

Van Kaam, R. C., Van Putten, M. J., Vermeer, S. E., & Hofmeijer, J. (2018). Contralesional brain activity in acute ischemic stroke. *Cerebrovascular diseases, 45(1-2), 85-92.*

Farewell lunch at an Ethiopian restaurant with part of the Hummel lab. Very delicious food and nice company.