Re-Connecting the Motor Brain in ALS with Electrical Stimulation

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Background

- Daily functional tasks result from complex communication between different regions of our brain - Functional Connectivity (FC).
- FC patterns are observed in several motor dysfunctions, originated by diseases such as Amyotrophic Lateral Sclerosis (ALS) [1].
- Cortical degeneration in ALS has been associated with aberrant patterns of FC detected by resting state encephalography (rs-EEG) [2].
- Transcranial direct current stimulation (tDCS) can modulate motor, sensory and cognitive functions in healthy subjects and patients with sensorimotor and psychiatric dysfunctions [3,4]. Also, tDCS has low costs and side effects, is well tolerated and portable.
- Electrodes' number, geometry and position can influence electric patterns induce by tDCS, resulting in different outcomes in FC [6].
- Computational tDCS modelling combined with EEG information can help to optimize stimulation of specific dysfunctional FC pattern.
- Brain FC in ALS can provide rs-EEG signatures to mark disease progression and to measure outcomes of tDCS modulation [2,7].

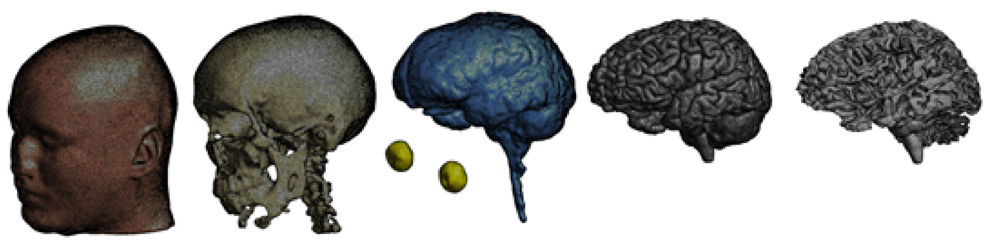
Research Questions

Does tDCS and tsDCS have the potential to repair/delay dysfunctional motor connectivity patterns in ALS?
What are the more effective stimulation settings?

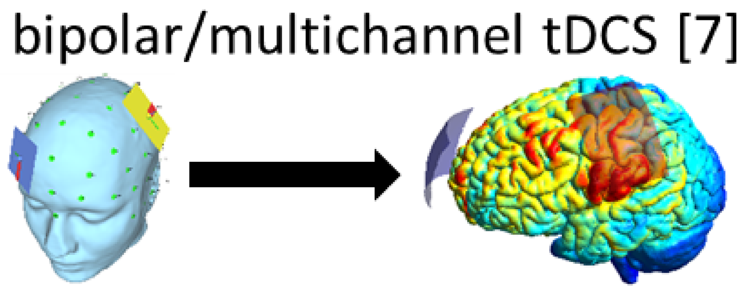
Project Overview

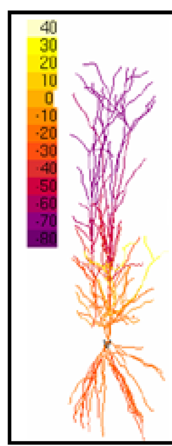
Creating the biophysical model

Volume conductor head model



Simulation of EF distribution due to bipolar/multichannel tDCS [7]





Biophysical models of cortical neurons (MN, IN, Synapses) [10]

EF effects on membrane potential and synaptic gains

Coupling of biophysical and physiological models NEURO-CONNECT-STIM MODEL

Generation of algorithms to optimize stimulation according to network target informed by rs-EEG database

Clinical validation of NEURO-CONNECT-STIM MODEL

Pilot studies in healthy volunteers
RCT in ALS patients with motor loss

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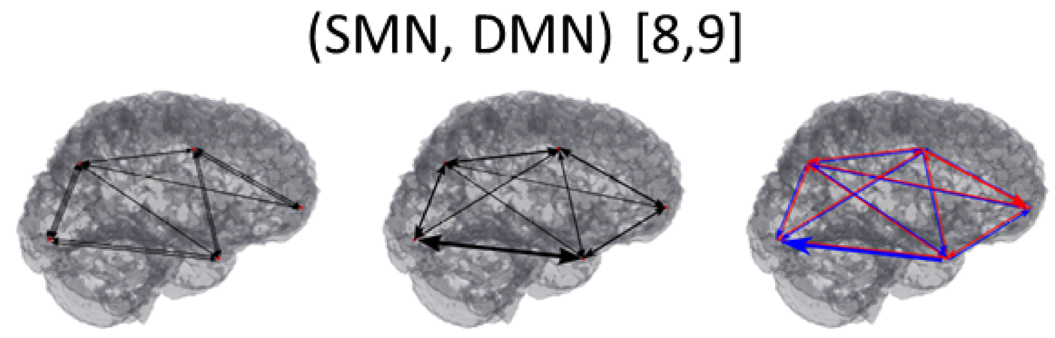
Creating the physiological model

Generation of database with rs-EEG patterns (SMN, DMN)

healthy subjects	baseline
ALS patients	sham/Active tDCS

Neural network model (SMN, DMN) [8,9]



Expected Outcomes

Demonstrate feasibility and efficacy of tDCS in the treatment of aberrant brain FC in ALS-induced motor dysfunctions.

Create a personalized-approach framework, with protocols informed by realistic models based on real FC data.

References

[1] Hallett et al., 2020, Clin Neurophysiol., 131(7):1621-1651. [2] Fraschini et al., 2016, J Physiol., 527(3):633-9. [4] Lefaucheur et al., 2017, Clin Neurophysiol., 128(1):56-92. [5] Fischer et al., 2017, Neuroimage. 2017 Aug 15;157:34-44. [6] Nasseroleslami et al., 2019, Cereb Cortex, 29(1):27-41. [7] Miranda et al., 2013, Neuroimage 70, 48-58. [8] Rodrigues et al., 2015, PeerJ 3, e923. [9] Ribeiro et al., 2015, PeerJ, 3:e1078. [10] Salvador et al., 2011, Clin Neurophysiol.,122(4):748-58.

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