Alzheimer Center Amsterdam
Amsterdam UMC

A Modelling Approach to Parameter Selection for Transcranial Direct Current Stimulation in Alzheimer's Disease

J. J. Luppi[a], W. de Haan[a]

ExMachina project

a. Department of Clinical Neurophysiology and MEG, Amsterdam Neuroscience, VU University Medical Center, Amsterdam UMC, The Netherlands

Background

- Counteracting the disrupted network activity in dementia due to Alzheimer's disease has the potential to treat the cognitive deficits that characterize the disease [1].
- Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that can be used to directly steer the activity in brain networks by modulating the excitability of targeted neuronal populations.
- The reproducibility of tDCS treatment effects remains a challenge, as there is no consensus on optimal stimulation parameters such as electrode placement, leading to arbitrary choices.
- We aimed to systematically generate theoretically optimized stimulation parameters through simulating their effects on spectral activity and functional connectivity in a well-established neural mass model.

Aim

To determine optimal stimulation parameters for a tDCS intervention in AD, based on simulated treatment outcomes in a neural mass model of the AD brain.

Methods

- The model in use is composed of neural masses, which consist of interconnected excitatory and inhibitory neurons, corresponding to 78 cortical regions. These regions are coupled to each other based on average human brain network topology. This is a computational model, with a set of algorithms that describe neuronal behavior, such as oscillations [2].
- We simulated the damaging effects of AD in this network using a previously reported activity-dependent degeneration (ADD) algorithm that produces AD-like damage [3] .
- The effects of tDCS were simulated by changing the excitability of pyramidal neurons in targeted neuronal masses at virtual time point 10. The affected neural masses are determined using current flow modelling (CFM) [4]. The setups were selected based on regions of interest in AD as well as current tDCS literature, resulting in 6 distinct setups, which were then reversed in polarity, hemisphere or both for a total of 20 setups.
- The outcome measures of choice were relative power in the lower and upper alpha band, total power, peak frequency, phase lag index (PLI) and amplitude envelope correlation (AEC), over virtual time. <u>Virtual stimulation strategies were considered successful when they were able to steer these outcome measures towards healthy control levels, in comparison to the ADD condition with no intervention (see Figure 1).</u>

Results

- The virtual tDCS elicited effects throughout the network and not just in the stimulated regions, affecting spectral power and functional connectivity. The best performers showcased a shift towards healthy control values and away from the ADD condition without intervention in all six outcome measures. In contrast, other setups resulted in little to no difference, while the worst setups even lead to further deterioration (see Figure 2 and Table 1).
- The two best performing setups were the two hemispheric variations of the of the occipito-frontal setup with anodal stimulation. On the 10-20 system of electrode placement, the positive anode was placed at either PO7 or PO8, while the negative cathode was placed at either AF4 or AF3 on the contralateral side (see Figure 2).
- Independent t-tests at virtual time points 10, 15 and 20 found significant shifts towards healthy control values for both occipito-frontal setups for all outcome measures in comparison to the ADD condition ($p < 0.001$). Independent t-tests between the occipito-frontal setups found that the right hemispheric variant outperformed the left hemispheric variant for example in relative power in the lower alpha band and PLI ($p < 0.05$), with no significant differences favoring the left hemispheric variant in any outcome measures.
- Our results indicate that the right hemispheric variant of the contralateral occipito-frontal setup with anodal stimulation best counteracts the disrupted network activity in AD. This prediction will be tested in a following clinical phase of the project via simultaneous magnetoencephalography during tDCS in AD patients.

Conclusion

Based on a systematic, model-guided analysis of tDCS stimulation setups, we found that anodal stimulation of the right occipital lobe with a contralaterally placed supraorbital cathode is theoretically optimised to counteract the network activity disruptions in AD.

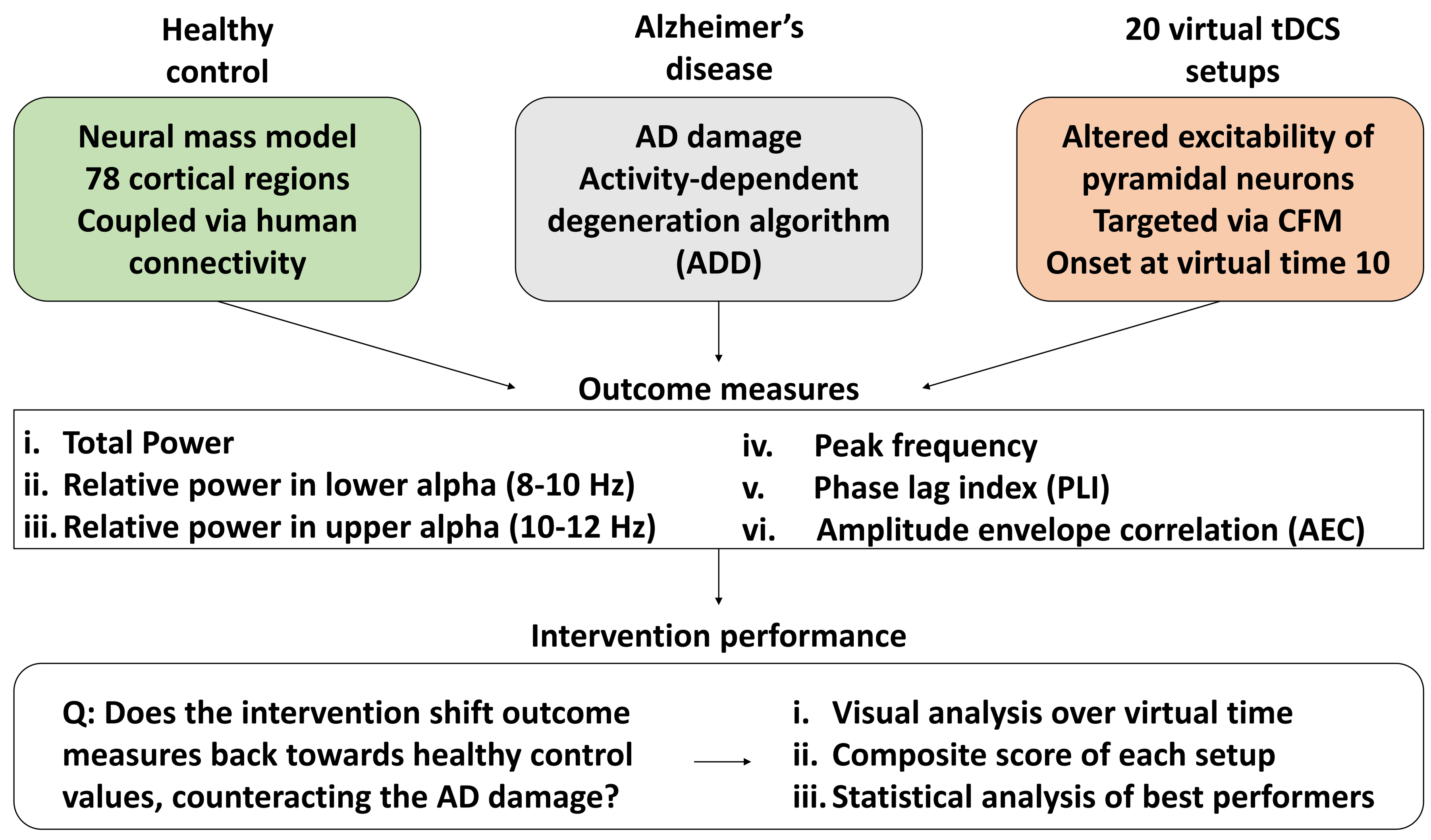

Figure 1: Experimental setup and definition of intervention performance

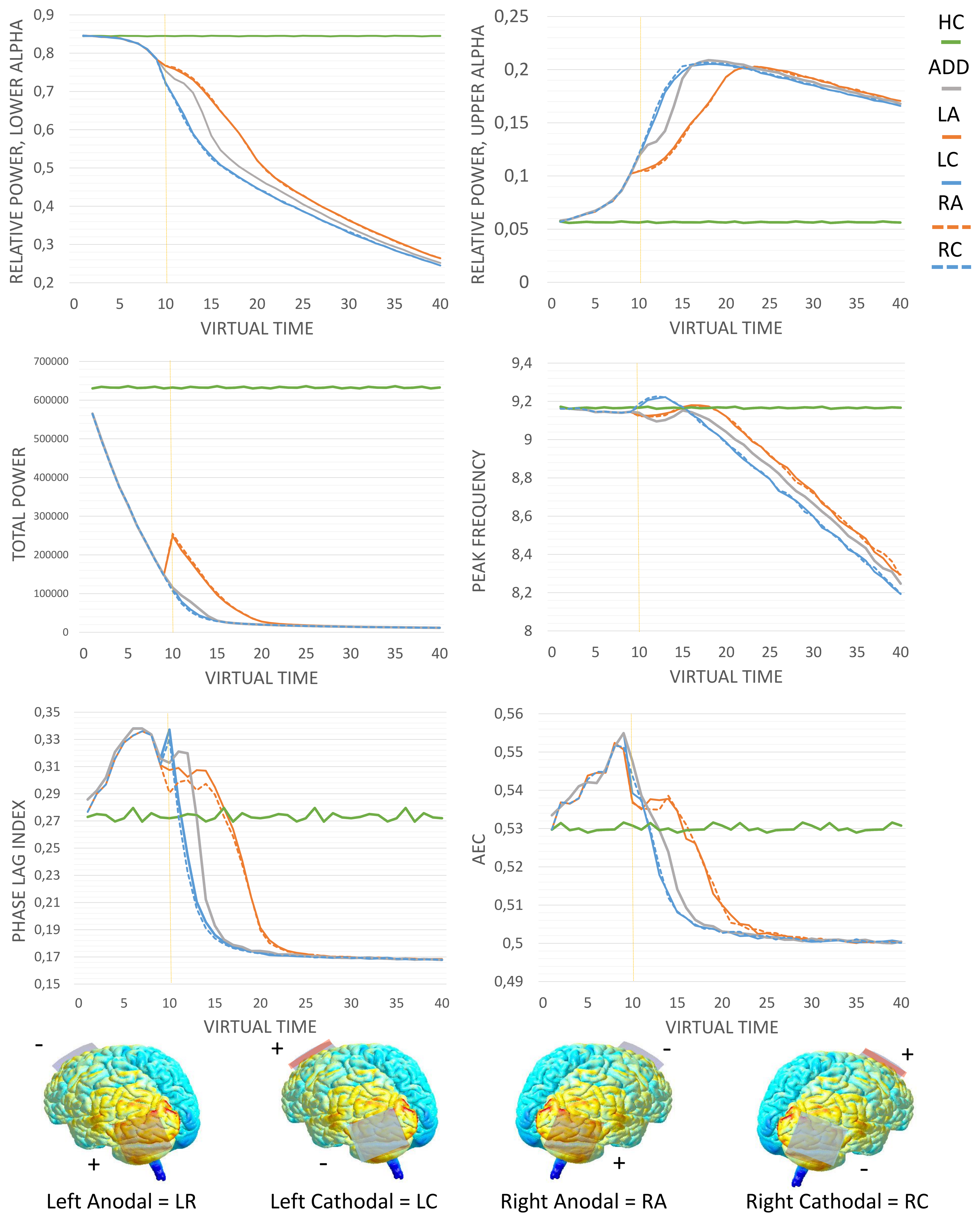

Figure 2: Outcome measures of the occipito-frontal setup over virtual time. Intervention onset was set at virtual time point 10. Figures are based on data averaged over 100 simulations, most differences are therefore significant although not shown for legibility.

Table 1: Composite scores of best and worst performing setups. Each outcome measure was scored either -1, 0 or 1, depending on the presence and direction of change from ADD values.

Setup	Variant	Score	Alpha1 (8-10 Hz)	Alpha2 (10-12 Hz)	Total Power	Peak Freq.	PLI	AEC
	Left anodal	6	1	1	1	1	1	1
	Left cathodal	-6	-1	-1	-1	-1	-1	-1
Occipito-	Right anodal	6	1	1	1	1	1	1
frontal	Right cathodal	-6	-1	-1	-1	-1	-1	-1
	Left anodal	5	1	1	1	1	0	1
	Left cathodal	-3	-1	0	1	-1	-1	-1
Temporo-	Right anodal	5	1	1	1	1	0	1
frontal	Right cathodal	-1	-1	1	1	-1	-1	0
Bilateral	Left anodal	6	1	1	1	1	1	1
posterior	Right anodal	6	1	1	1	1	1	1

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Amsterdam Neuroscience
ZonMw
j.j.luppi@amsterdamumc.nl