Neural Interaction Dynamics Between the Anterior Thalamus and the Cortex in Epilepsy Patients

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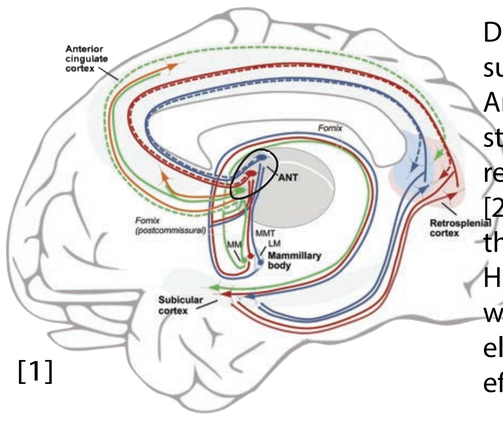
INTRODUCTION



[1]

Due to its connectivity profile to cortical regions and its suggested role in the subcortical propagation of seizures, the Anterior Nucleus of the Thalamus (ANT) is chosen as the stimulation target in Deep Brain Stimulation (DBS) for drug - resistant epilepsy (DRE) [1,2]. Although response rate is high [2], some patients still do not benefit significantly from this therapy, and mechanisms of efficacy are yet to be explored. Here, we aimed to analyze how the ANT functionally interacts with the neocortex and to shed light on some of the electrophysiological mechanisms underlying the effectiveness of this method.

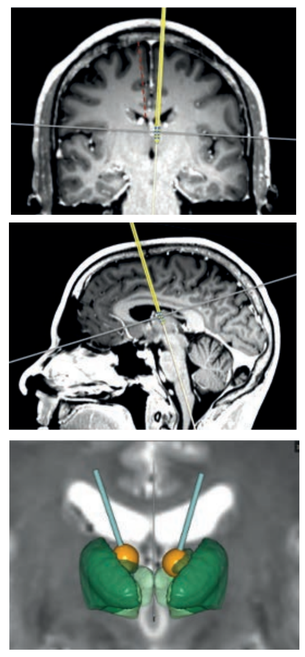
MOTIVATION

- **1a** Define the electrophysiological properties of the ANT
- **1b** Characterize the functional connectivity of the ANT to scalp regions
- **2** Explore changes in the cortical neural activity during high frequency stimulation of the ANT
- **3** Find intra-operative neural biomarkers of responsiveness to therapy

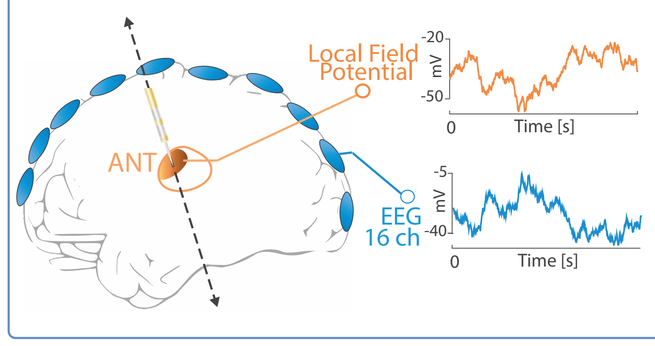
METHODS

ANT-DBS IMPLANT

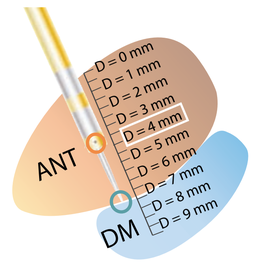
15 DRE patients



1: ANT-SCALP RECORDING

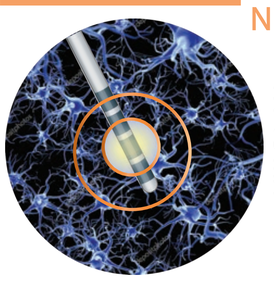


DEPTH RECORDINGS



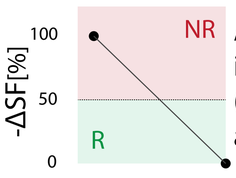
2: TEST STIM

N = 11



PF: 135 | 145 Hz
PA < 3 mA

3: RESPONSIVENESS TO THERAPY

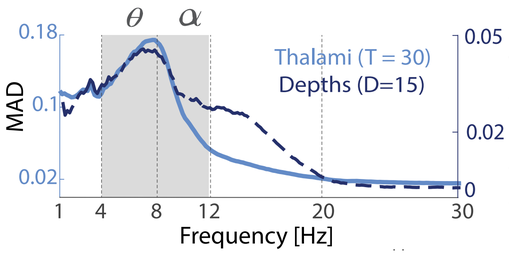


Assessed as the % change in Seizure Frequency (ΔSF) from baseline, with a threshold ΔSF = -50%.

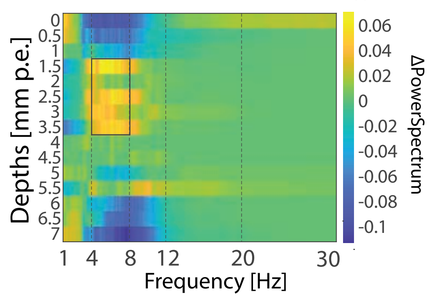
1: THE ANT-SCALP CONNECTIVITY IS MOSTLY DRIVEN BY θ OSCILLATIONS AT FRONTO-CENTRAL REGIONS

The connectivity between the scalp and the ANT is driven by θ oscillations, independent on the depth of recording and focused on ipsilateral fronto-central regions.

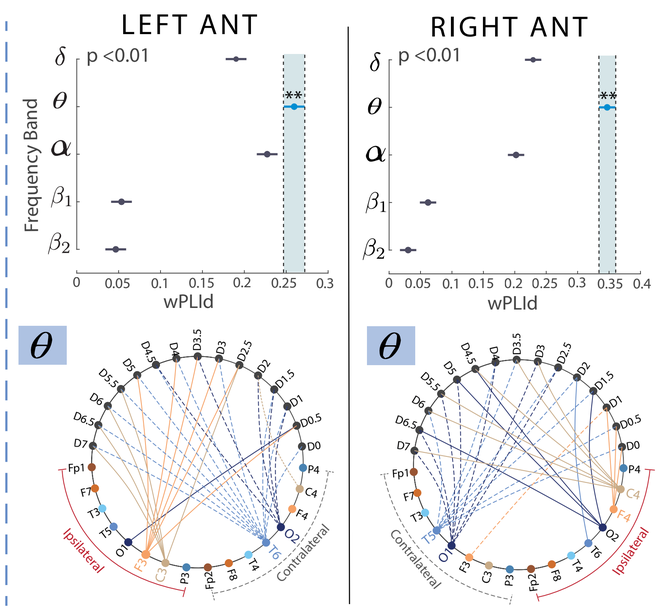
1a: ANT ELECTROPHYSIOLOGY



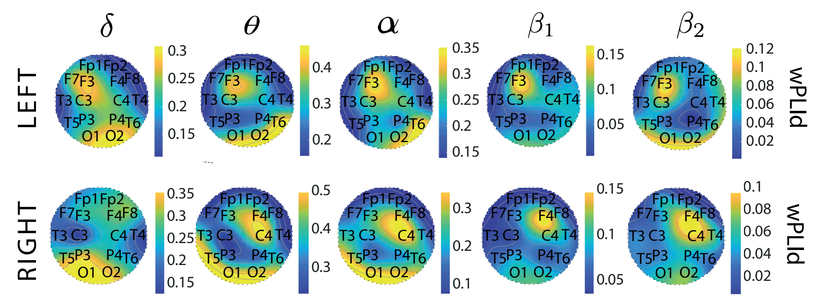
The major difference among thalami was observed in the θ and low-α range. The same result was found along the implantation trajectory.



A sweet-spot of higher θ power was found at approximately 1.5 to 3.5 mm post-entry.



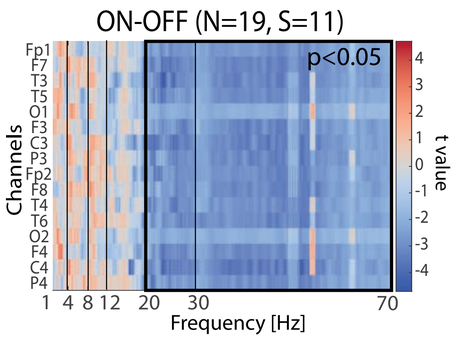
1b: ANT-SCALP CONNECTIVITY



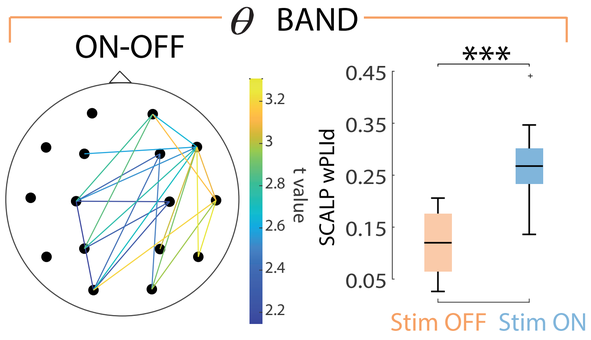
The highest interaction between the ANT and the scalp is at θ (ANOVA, p<0.01). Possibly underlying the anatomical connection of the ANT to the ACC and the RSC, this interaction is focused on fronto-central regions on the ipsilateral side and temporo-occipital regions on the contralateral side. Finally, we could assess that the depth of recording in the ANT does not affect the profile of connectivity in any frequency band.

2: DBS INDUCES SIGNIFICANT CHANGES IN SCALP ELECTROPHYSIOLOGICAL MARKERS

Acute ANT stimulation shifts the power spectrum towards lower frequencies and increases scalp connectivity in θ.



A significant reduction in higher frequencies (β2 and γ) spread throughout the scalp was found when DBS was ON, counteracted by a trend towards an increase in lower frequencies (not significant).

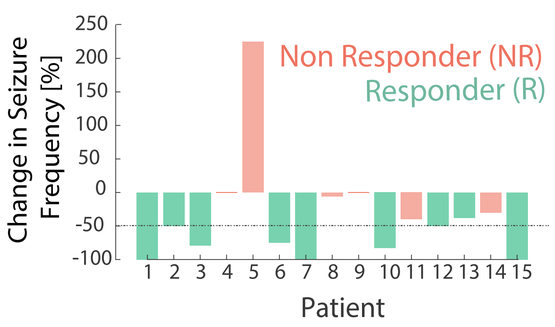


No statistically significant reduction in scalp connectivity was present when DBS was ON.

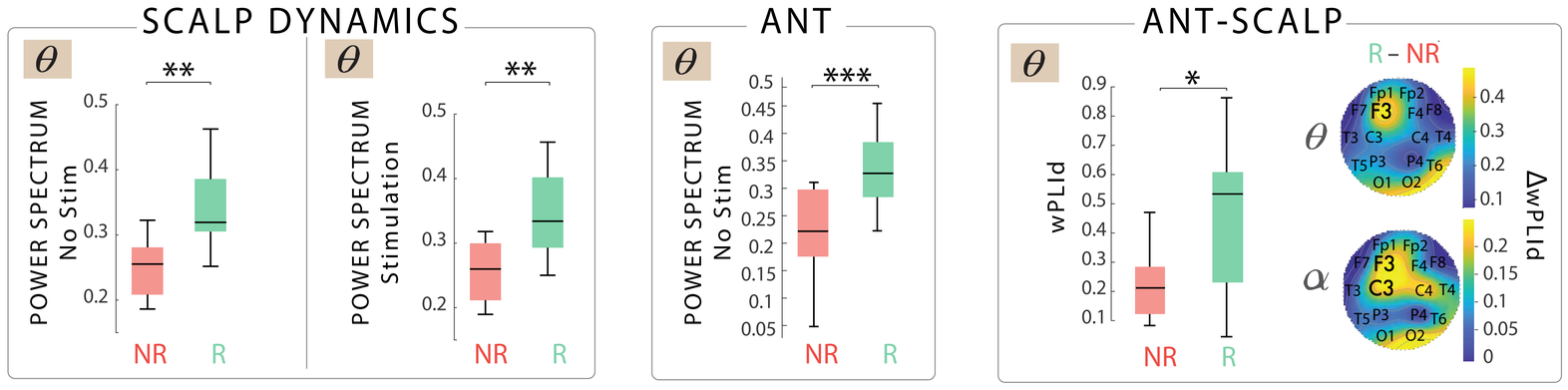
A significant increase of the scalp connectivity between the highlighted regions in the θ frequency band could be found.

3: ANT- SCALP NEURAL PROPERTIES CAN PREDICT OUTCOME TO THERAPY

θ power at ANT and scalp (ON | OFF) positively correlates with therapy outcome. An increased ANT-SCALP connectivity in θ at fronto-central regions is present in Responders.



We divided the patients into Responders (N=9) and Non Responders (N=6) by assessing the change in Seizure Frequency from baseline to 6 months post implant.



Responders presented a significantly stronger scalp and ANT θ power, both in ON and OFF conditions . The average ANT-Scalp θ connectivity was stronger in Responders than in Non Responders, with a focus on F3/C3. Relative changes caused by ANT stimulation, both in scalp power spectrum and in scalp connectivity, did not present significant correlation with responsiveness to therapy, suggesting that observing the acute intra-operative effect of DBS on scalp dynamics does not provide meaningful insights into therapy's success.

CONCLUSIONS

- **1a** The θ and low-α band is where the highest variability of ANT electrophysiological properties among subject/depths is found.
- **1b** The ANT-scalp connectivity is driven by a fronto-central θ connectivity.
- **2** DBS induces a decrease of higher-band power and increases the scalp connectivity at θ in a statistically significant manner.
- **3** Subjects with a higher scalp θ power in ON/OFF and higher θ power in the ANT are more likely to be responsive to therapy. ANT-Scalp θ power connectivity also correlates positively to responsiveness.

REFERENCES

[1] Salanova V et al. Neurology 2015; 1017-1025
[2] Fisher R. et al. Epilepsia 2010; 899-908

ACKNOWLEDGMENTS

This work was supported by an SNSF Project Grant to Rafael Polania and Lukas Imbach.

Swiss National Science Foundation