Patients with Isolated RBD at higher risk of phenoconversion exhibit steeper slopes of the EEG arrhythmic component

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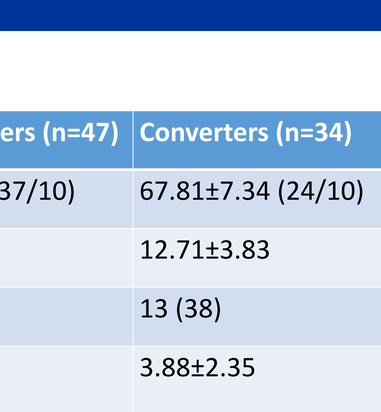
Introduction

iRBD → prodromal stage of clinical synucleinopathies, including Parkinson's disease (PD) and dementia with Lewy body (DLB)

Standard estimation of spectral power fails to identify resting-state EEG markers discriminating patients at higher risk of phenoconversion

New paradigm →



Arrhythmic component:

- Scale-free 1/f$^{\beta}$ power law
- The steepness of the slope is informative about large neuronal population's dynamics

Objective: Estimate the slope of the arrhythmic component to determine if it differ between iRBD patients who converted towards a synucleinopathy and those who remained disease-free

Hypothesis: Converters will exhibit steeper slopes of the arrhythmic component as previously reported in PD and DLB

Method

Sociodemographic

	Non-converters (n=47)	Converters (n=34)
Age (M/F)	65.53±7.09 (37/10)	67.81±7.34 (24/10)
Education	13.68±3.78	12.71±3.83
MCI, n (%)	16 (34)	13 (38)
Follow-up (years)*	5.91±2.77	3.88±2.35
MDS-UPDRS-III*	3.25±2.99	6.29±3.65

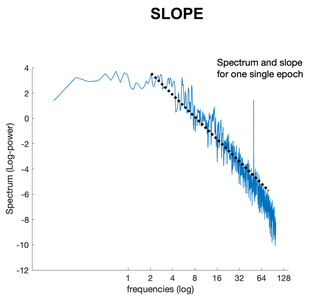
Data analysis:

Spectral power over 4s epochs

- Electrodes: F3,F4,C3,C4,P3,P4,T3,T4,O1,O2

Arhythmic component

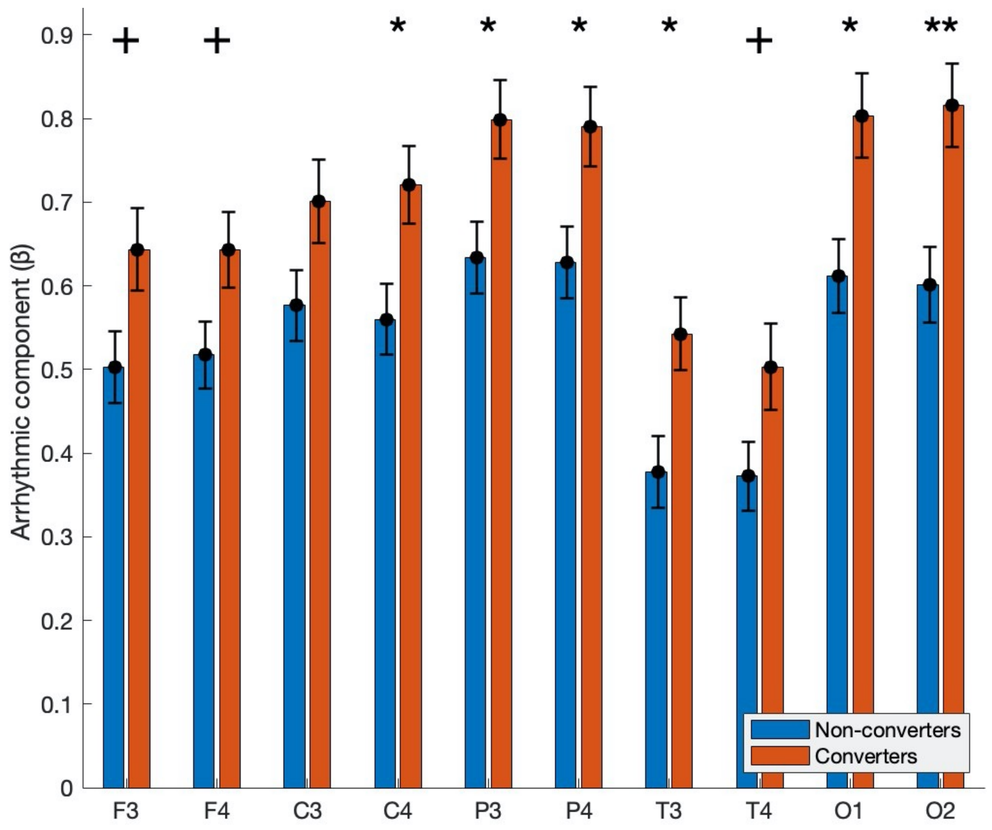
- 1/*f* regression curve computed in log-log space (see introduction)
- Extraction of the scaling exponen and average across epoch for each electrodes



Statistical analysis:

- Permutation test with a pixel-based correction for slope value differences across all electrodes (2000 permutations)
- MATLAB custom script

Results

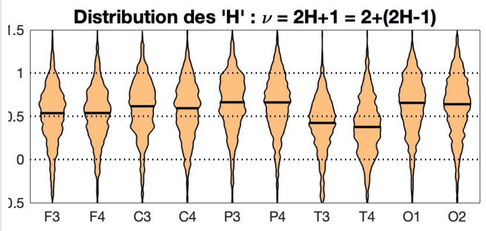


Electrode	Non-converters (n=47)	Converters (n=34)
F3	0.5027 ± 0.0424	0.6434 ± 0.0491
F4	0.5172 ± 0.0403	0.643 ± 0.0447
C3	0.5766 ± 0.0424	0.7012 ± 0.0499
C4	0.5599 ± 0.0424	0.7208 ± 0.046
P3	0.6338 ± 0.0428	0.7989 ± 0.0474
P4	0.6278 ± 0.0425	0.7902 ± 0.0481
T3	0.3774 ± 0.0434	0.5421 ± 0.0435
T4	0.3726 ± 0.041	0.5032 ± 0.0513
O1	0.6113 ± 0.0442	0.8034 ± 0.0507
O2	0.6011 ± 0.0449	0.8159 ± 0.0501

Table 1: Descriptive data for slope values. iRBD patients who remained disease-free (non-converters) are shown in the second column and those who were diagnosed with a synucleinopathy (converters) are shown in the third column. Value are represented as mean ± standard error.

Figure 1: Slope of the arrhythmic component in converters (red bars) and in non-converters (blue bars) for each electrode. The y-axis shows the slope of the arrhythmic component, as represented by the scaling exponent βi. Statistically significance differences are identified by * ($p < .05$) or ** ($p < .01$). Statistical trends are labeled by + ($0.05 < p < 0.1$). Error bars represent standard error.

Non-Converters



Converters

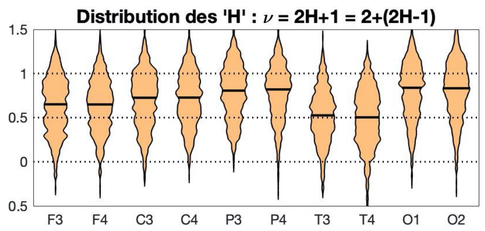


Figure 2: Distribution of values for the slope of the arrhythmic component for non-converters (left) and converters (right)

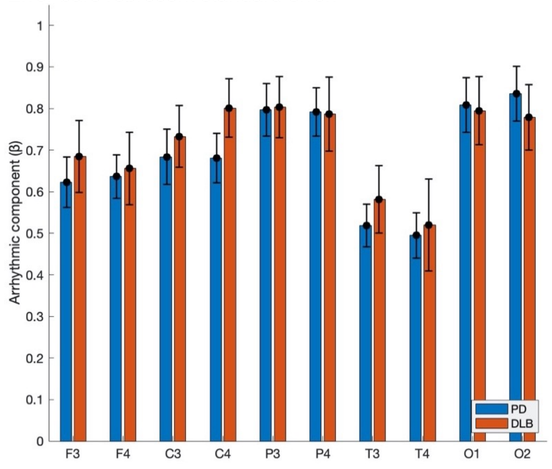


Figure 3: Slope of the arrhythmic component in patients who were diagnosed with PD (blue bars) and those who were diagnosed with DLB (red bars) for each electrode.

Discussion

Summary

Patients with iRBD who phenoconverted towards a clinical synucleinopathy exhibit steeper slopes of the arrhythmic component across many electrodes, but most predominantly in posterior regions (Figure 1). When comparing converters on the clinical trajectory (i.e. PD or DLB), we don't find any significant differences (Figure 3).

Interpretation

- Synucleinopathy differs from healthy aging where the slope of the arrhythmic component ten to flatten
- Excitatory-to-inhibitory ratio (E:I ratio) hypothesis: steeper slopes are indicative of a lower E:I ratio.
    - iRBD has been linked to altered activity of glutamatergic neurons in the subcoeruleus leading to hyperactivation of GABAergic neurons in the ventromedial medulla
    - As the synucleinopathy progresses rostrally, subcortical hubs become increasingly affected, leading to temporal disorganisation of cortical networks = ↑ arrhythmic activity

- Patients with PD and with DLB have been shown to exhibit steeper slopes as compared to patients with MCI and healthy controls
    - Similarly, patients with AD and healthy controls seem to show similar slope values

References

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Acknowledgments

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