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Combined EEG and ERG Features for Bipolar Disorders Diagnosis

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2023 : Master's degree in Statistics, Modeling and Data science from the University Claude Bernard Lyon 1, France.

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- Under the supervision of Valerie Louis Dorr and Steven Le Cam
- Mathematics and Signal processing

Team Signals and Models for Neurosciences (SiMoNe)

- Methods for the diagnosis of cognitive, neurological or psychiatric disorders
- Develop computational models of these disorders
- **Analysis electroencephalogram (EEG) and electroretinogram (ERG) responses to light stimuli in order to differentiate patients with bipolar disorders (BD) from control subjects.**

Bipolar disorders (BD) are mood disorders …

(Hypo)Manic state	Euthymic state	Depressive state
Abnormally elevated or irritable mood	**Relatively stable mood**	**Low or depressed mood**

… difficult to be diagnosed.

Interview conducted by psychiatrist based on the Diagnostic and Statistical Manual (DSM-V) for bipolar disorders (symptoms, family medical history)

➡ Subjective diagnosis

People with BD are more likely to seek help during the depressive state

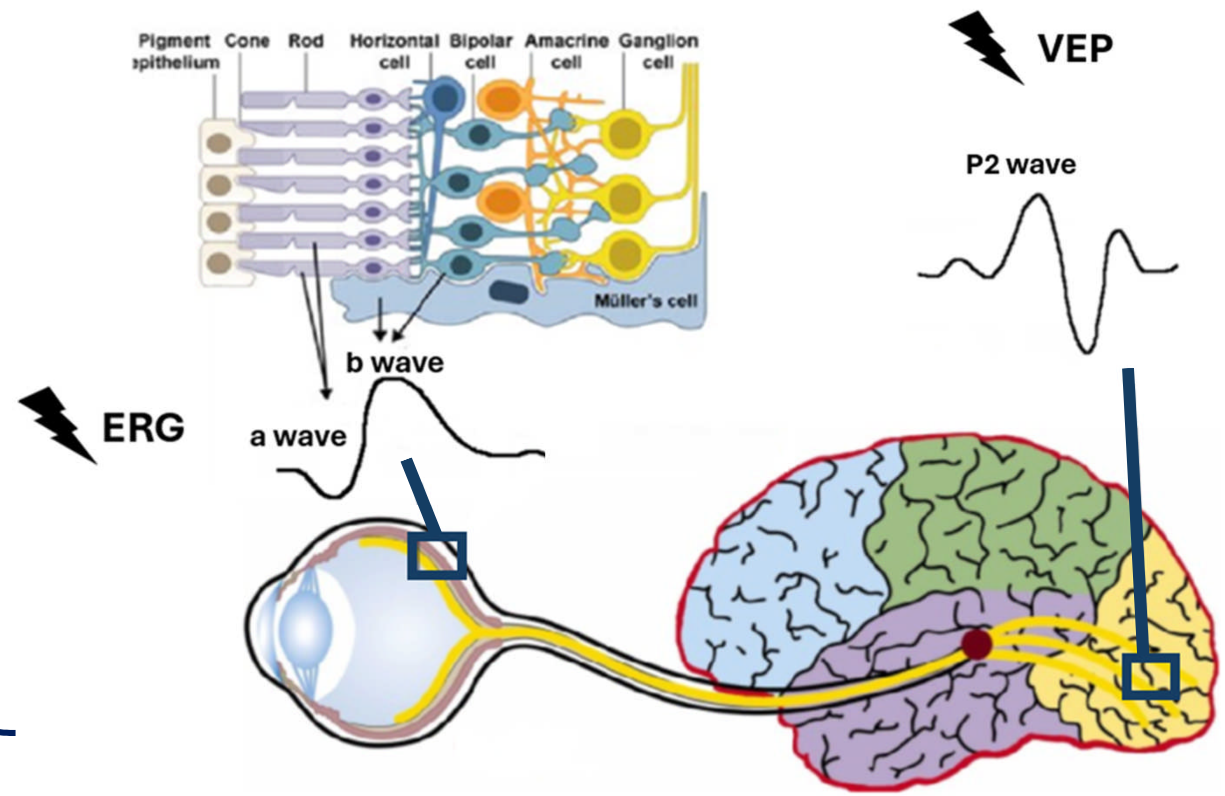
➡ Misdiagnosed with depression

- ❖ A average delay of 10 years between the first symptoms and the diagnosis
- ❖ A need for objective sensitive and specific biomarkers

Context

Electroencephalogram (EEG) alterations in responses to Visual Evoked Potentials (VEP) recorded from primary visual cortex areas are also well-documented [7]

- Full-field electroretinography : light flashes to assess the bioelectrical activity of retinal cells.
- Previous studies have shown that psychiatric disorders in general affect the responses of retinal rod and cone cells [2-4]
- Electroretinigram (ERG) responses to light stimuli can help in the differential diagnosis of mental disorders [5,6]



The aim of this study is to assess the benefit of combining ERG with EEG measurements for Bipolar Disorder (BD) diagnosis using a supervised machine learning model.

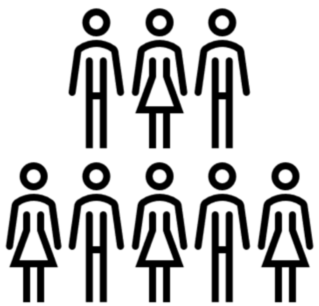
Study protocol

Population from BiMAR study [1]

Patients with BD (euthymic state)

N = 30
Age = 47.5 +/- 13.3
Women = 68 %

Control



N = 25
Age = 42.3 +/- 14.8
Women = 60 %

Matched for age and sex

Retinaute device

Virtual reality headset equipped with electrodes

Displays

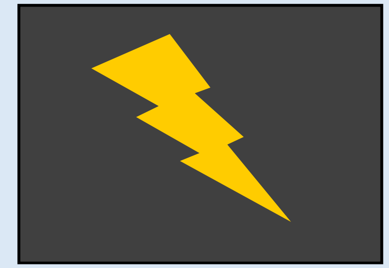
Flash stimulations

Flash intensity : 3 cd.s.m^{-2}

Light-adapted (LA)

LA3.0 (32 flashes)
30Hz Flicker (16 flashes)

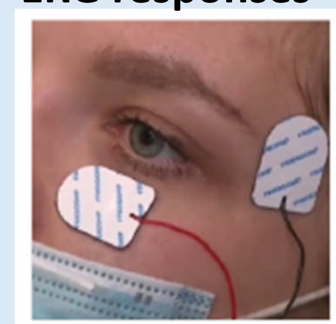
Dark-adapted (DA)



DA3.0 (16 flashes)

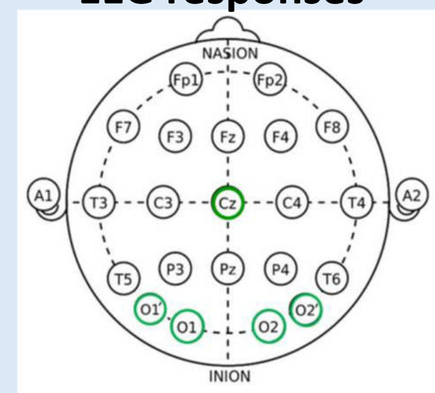
Records simultaneously

ERG responses



Bipolar derivation for each eye (skin electrodes)

EEG responses



4 electrodes on the occipital lobe, reference in Cz

Signals preprocessing (1/2)

A Signals Filtering

Sampling frequency = 1000 Hz

1. Powerline noise removal

Notch filter

- center frequency = 50Hz
- quality factor = 5

2. Band-pass Filter [1-62,5] Hz

Using discrete wavelet transform (DWT) :

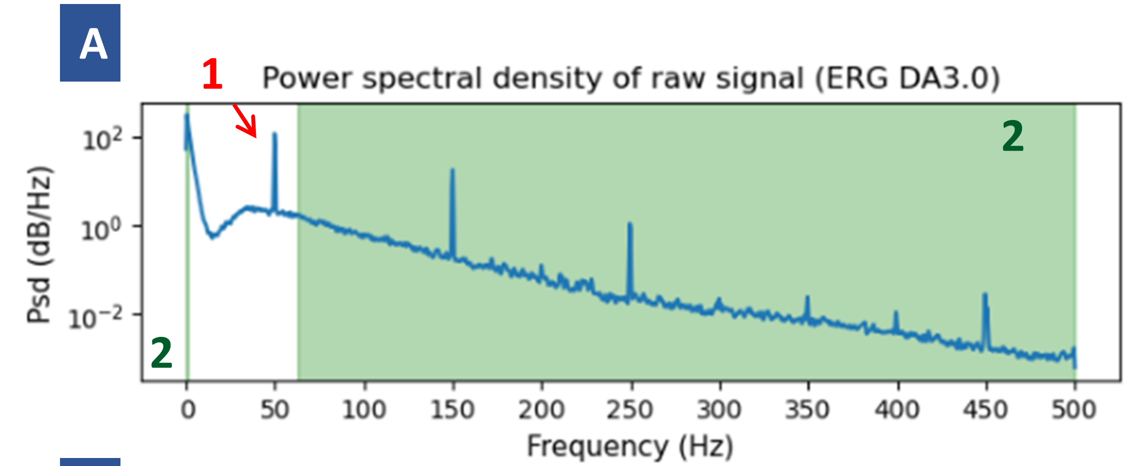
- Daubechies-6 wavelet
- 10-level decomposition

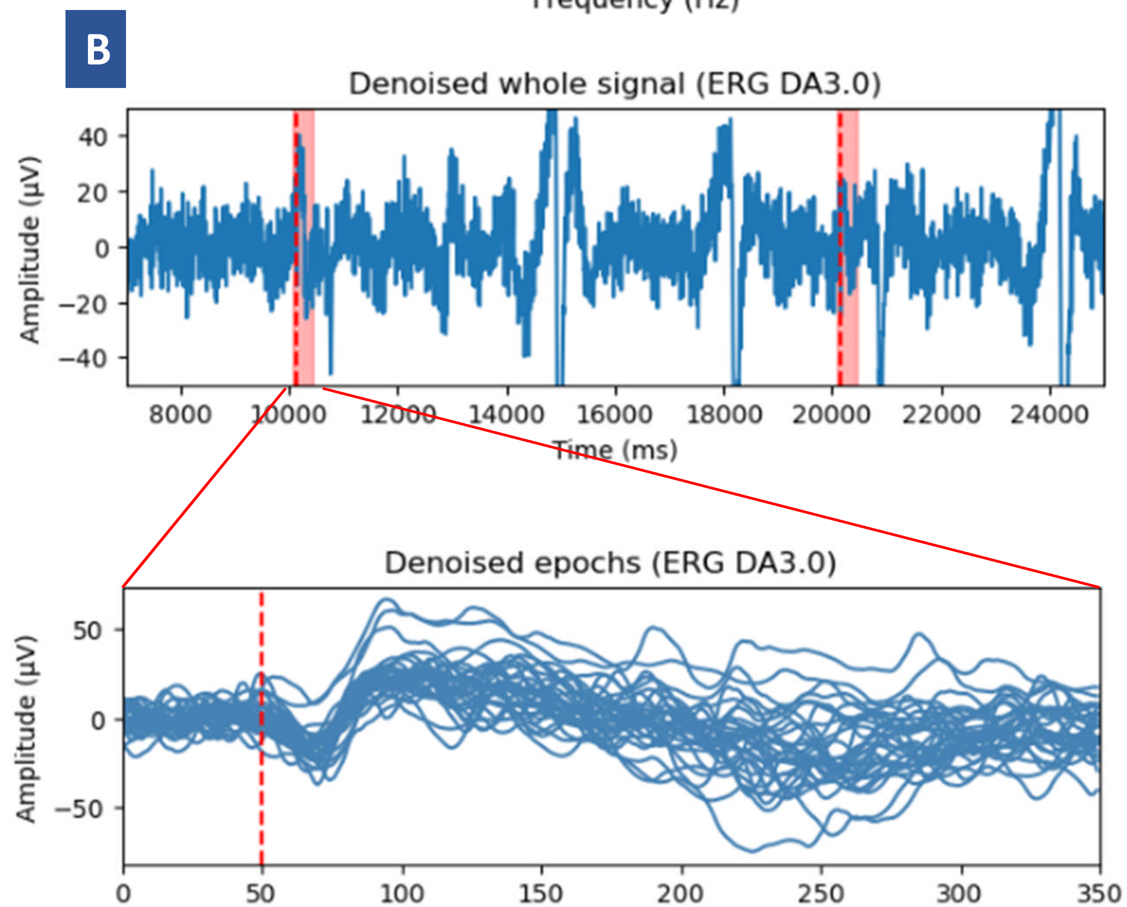
Coefficient	Frequency range (Hz)
D1	**[250, 500]**
D2	**[125, 250]**
D3	**[62.5, 125]**
D4	[31, 62]
D5	[16, 31]
D6	[8, 16]
D7	[4, 8]
D8	[2, 4]
D9	[1, 2]
A9	**[0, 1]**

Low frequencies (0-1 Hz) and high-frequencies (>= 62.5 Hz) filtered.

B Segmentation in epochs

	ERG	EEG
Start	50 ms before flash	
End	300 ms after flash	400 ms after flash





Signals preprocessing (2/2)

C **Removal of outliers**

For each stimulus, all ERGs (left and right) are gathered, all EEGs (O1, O1’, O2, O2’) are gathered.

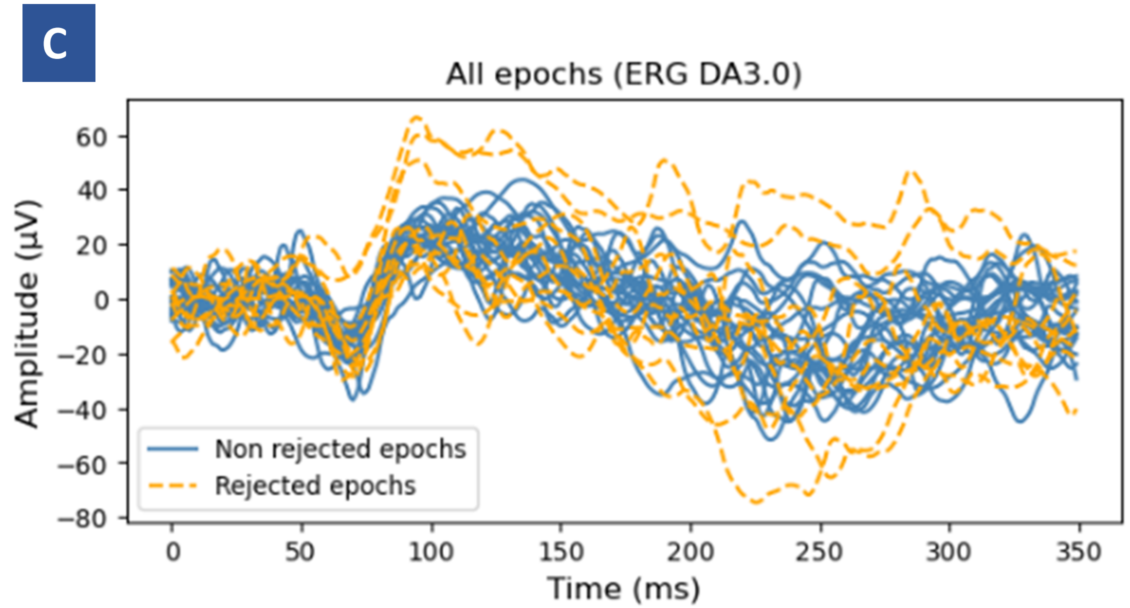
Principal component analysis performed for each modality (each epoch is an individual).

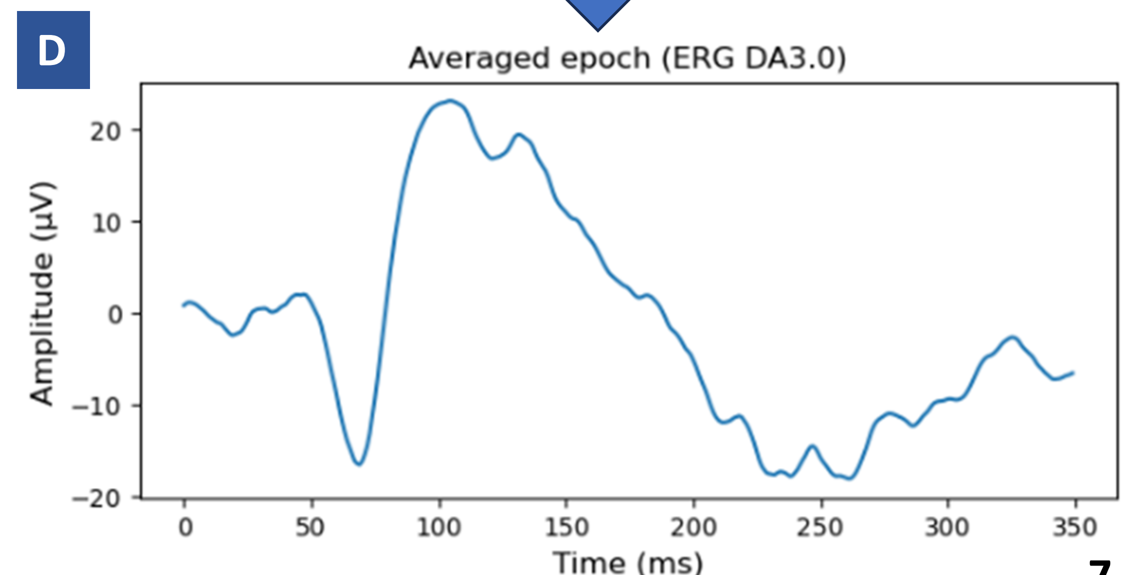
Outlier = points outside the [10%, 90%]-percentile range for at least one of the first three components

Rejected epochs (%)	ERG	EEG
DA3.0	10-30	10-25
LA3.0	10-30	15-25
Flicker	15-30	15-30

D **Averaged epoch**

Non rejected ERG epochs are averaged.
Non rejected EEG epochs are averaged.





Feature selection : time domain

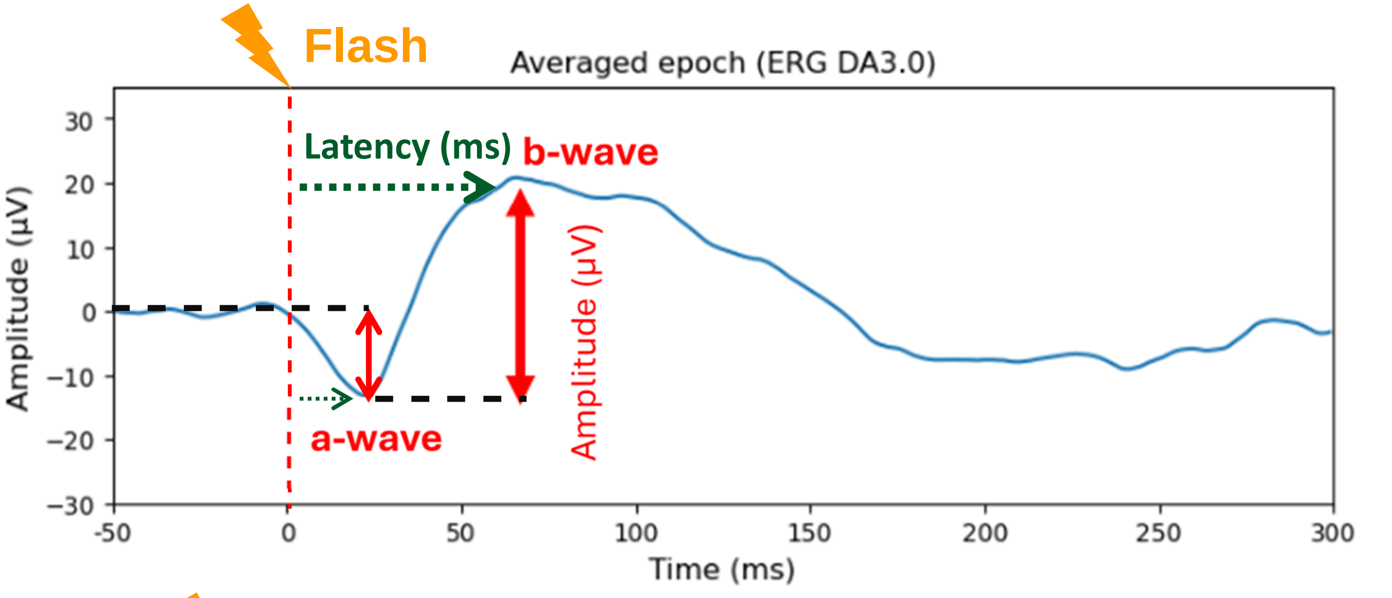
Features

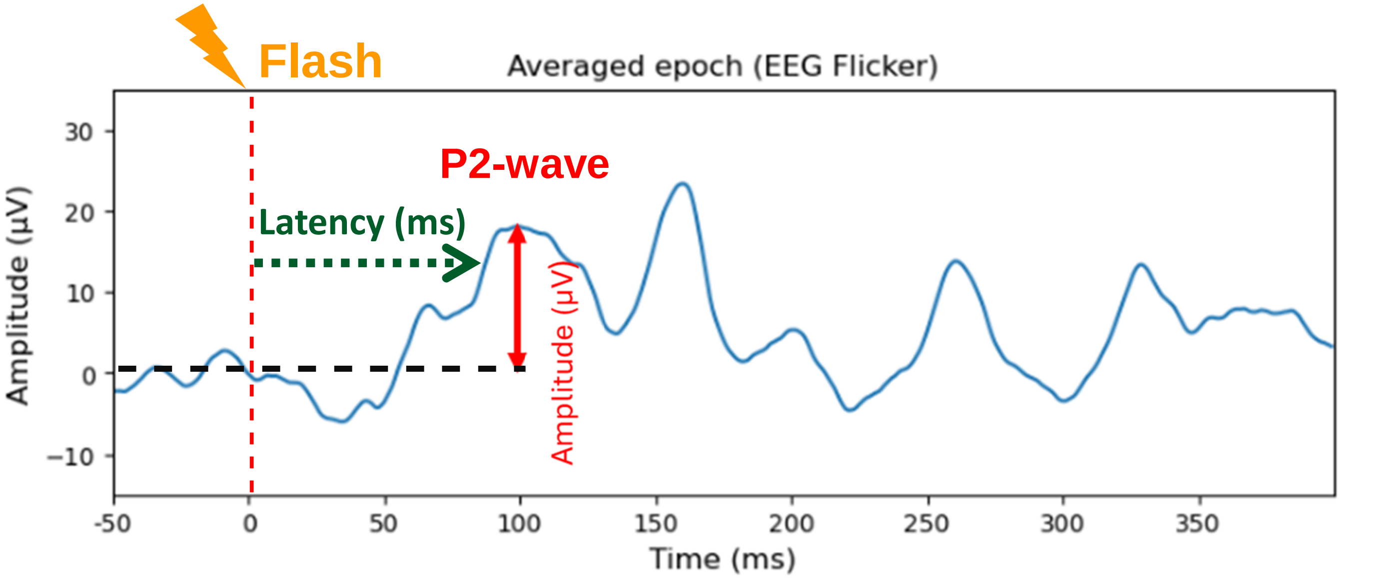
We measured P2 wave (EEG) / a and b waves (ERG) Amplitude and Latency.

a/P2 wave amplitude : from baseline to trough/peak

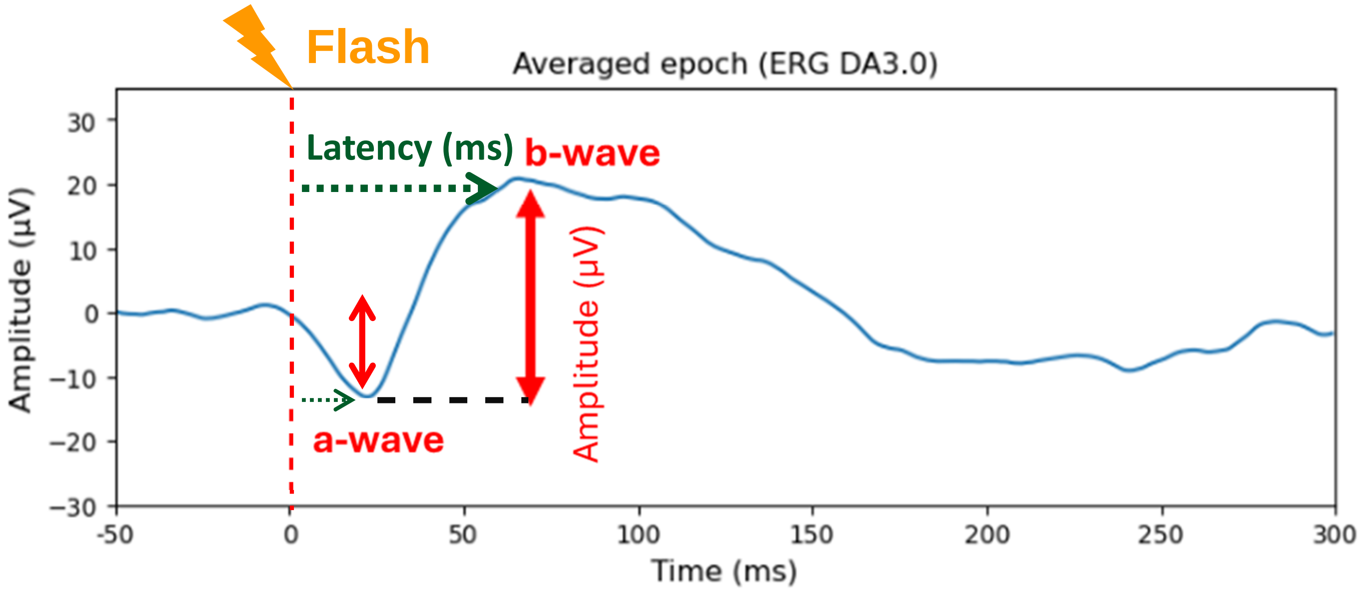
b-wave amplitude : from a-wave trough to b-wave peak (by convention)

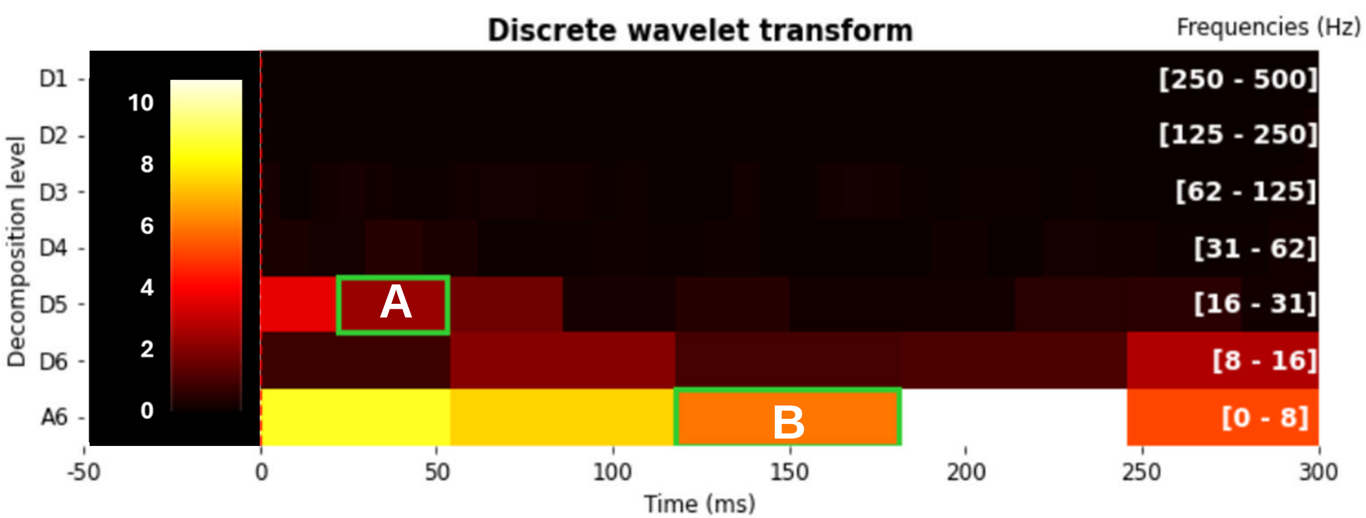
Latency (or Peak time) : time from flash and peak/trough





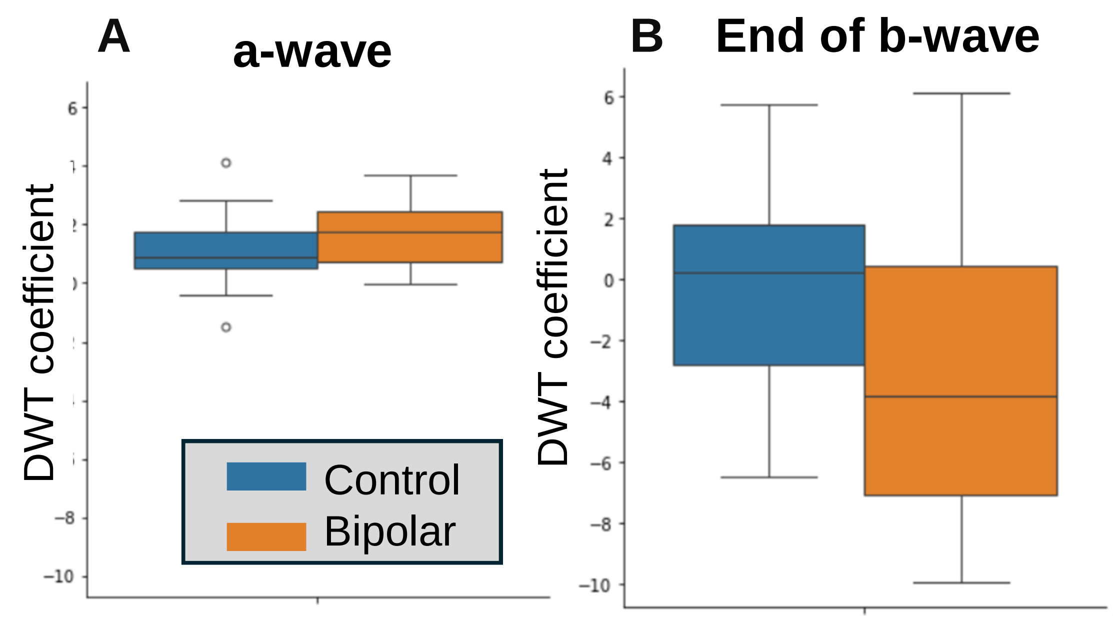
Feature selection : time frequency domain





Features

DWT with **daubechies-4** wavelet and **6-level decomposition**.



Selected Features

Statistical test

Select features significantly different between patients with BD and the control population

- Wilcoxon ranksums test
- alpha risk < 0.05 (by convention)

Time domain

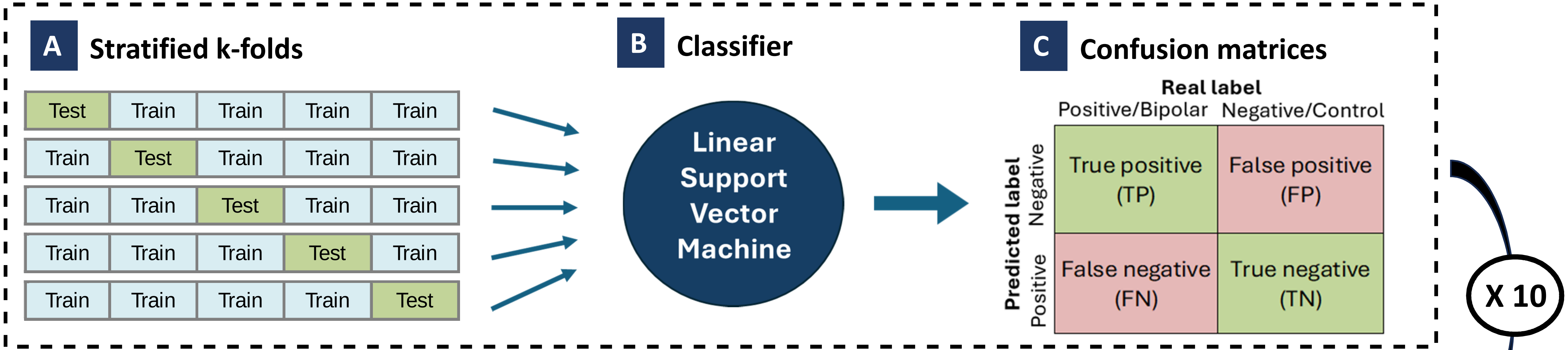
Stimulus	Origin	Feature	Wilcoxon test
DA3.0 ERG	a-wave	Amplitude	$p < 0.05$
LA3.0 ERG	a-wave	Latency	$p < 0.05$
Flicker EEG	P2-wave	Amplitude	$p < 0.01$

Time frequency domain allows us to extract more significant features for each stimulus and modality

Time frequency domain

Stimulus	Origin	Frequency	Wilcoxon test
DA3.0 ERG	a-wave	[16-31] Hz	$p < 0.05$
DA3.0 ERG	b-wave	[0-8] Hz	$p < 0,05$
LA3.0 ERG	b-wave	[16-31] Hz	$p < 0.01$
Flicker ERG	Trough 1	[16-31] Hz	$p < 0.05$
Flicker ERG	Trough 7	[31-62] Hz	$p < 0.05$
Flicker ERG	Peaks 6-7	[8-16] Hz	$p < 0.05$
LA3.0 EEG	P2-wave	[8-16] Hz	$p < 0.05$
Flicker EEG	P1-wave	[0-8] Hz	$p < 0.01$
Flicker EEG	N3-wave	[16-31] Hz	$p < 0.05$

Supervised machine learning model



- Divide the subjects into k groups (k= 5, 11 subjects ; 6 Bipolars, 5 Controls ; in each group)
- For each i^{th} iteration : Linear Support vector machine is trained on 4 folds (44 subjects) and predictions are made on the remaining fold (11 subjects)
- Each prediction results in number of True positives (Bipolars), False positives, False negatives and True negatives (Controls).
- We repeated this operation 10 times with new 5-folds.

D **Averaged scores**

Accuracy $= \frac{1}{K}\sum_{1}^{K}\frac{TN+TP}{TN+TP+FN+FP}$

Recall $= \frac{1}{K}\sum_{1}^{K}\frac{TP}{TP+FN}$

Specificity $= \frac{1}{K}\sum_{1}^{K}\frac{TN}{TN+FP}$

F1 score $= \frac{1}{K}\sum_{1}^{K}\frac{2TP}{2TP+FN+FP}$

Classification results

Electrode	Feature	F1_score (mean (SD))	Accuracy	Recall	Specificity
EEG	Time	65.4 (12.8)	60.2 (11.3)	72.7 (21.0)	45.2 (20.5)
	Time-frequency	75.5 (12.3)	73.1 (14.0)	76.7 (15.8)	68.8 (21.8)
ERG	Time	70.9 (10.1)	67.5 (11.3)	73.3 (13.9)	60.4 (20.4)
	Time-frequency	76.5 (11.4)	74.4 (10.3)	79.7 (17.3)	68.0 (15.1)
EEG/ERG	Time	74.4 (9.6)	68.4 (11.5)	84.7 (14.2)	48.8 (20.7)
	Time-frequency	**82.8 (9.2)**	**80.4 (10.1)**	**87.3 (12.9)**	**72.0 (15.7)**

- ❖ The results suggest that time-frequency features outperform classic time features in the discrimination of Bipolars/controls for any electrode.
- ❖ Combining EEG and ERG responses allows a more performant classification with greater scores and lower standard variations.
- ❖ Our model better discriminates Bipolars (average recall 87,3%) than Controls (average specificity 72%).

Conclusion and perspectives

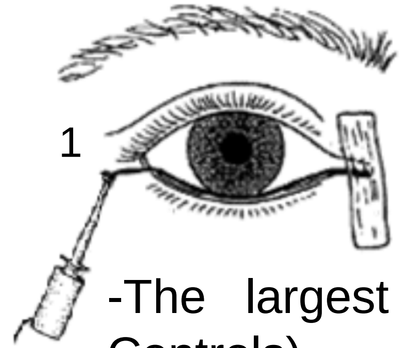
Our work

Wavelet coefficients of combined EEG/ERG can be used in diagnosing subjects with BD, and provide in particular high recall on average (87.3 %)

Skin electrodes for ERG

Lower amplitudes [8]

More user-friendly



1

Hébert et al., 2020

-The largest study to date (151 BD, 200 Controls)
- Time domain ERG features
- Accuracy = 89%, recall = 76%, specificity = 88 %

DTL electrodes for ERG

- Wavelet coefficients provide a more detailed representation of the ERG/EEG evoked potentials.
- The relatively small data set might limit the generalizability of the obtained results.

Future work :

- **Include clinical data and human expertise for a fully-integrated decision process.**
- **Include new flash stimuli to isolate other cells activity and increase discriminating**

1. https://iscev.org/tech/

Thank you for your attention

References

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