ANALYSIS OF ELECTROENCEPHALOGRAPHIC RECORDINGS FROM EPILEPSY PATIENTS USING RESTRICTED GRANGER CAUSALITY MEASURES

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Objective

Epilepsy is a chronic disorder of the brain that affects 1% of world population. The occurrence of epileptiform discharges (ED) in electroencephalographic (EEG) recordings of patients with epilepsy signifies a change in brain dynamics and particularly brain connectivity. In the last decade, many linear and nonlinear measures have been developed for the analysis of EEG recordings to detect the direct causal effects between brain regions. In many cases the number of EEG channels (the time series variables) is large and the analysis is based on short time intervals, resulting in unstable estimation of vector autoregressive models (VAR models) and subsequently unreliable Granger causality measure. For this, restricted VAR models have been proposed and in our recent study it was found that optimal restriction of VAR for the estimation of Granger causality was obtained by the backward-in-time selection method (BTS). We use the concept of restricted VAR models in measures both in time and frequency domain, namely restricted conditional Granger causality and restricted generalized partial directed coherence. We test the two measures in their ability of detecting changes in brain connectivity during an epileptiform discharge from multi-channel scalp electroencephalograms (EEG).

Data and Methodology

A. Summary of problem and solution

- **Granger causality** measures: quantify statistical causal relationships among the observed variables.
- **conditional Granger causality index (**CGCI): measures **direct** causal effects from one variable (EEG channel) to the other accounting for the remaining observed variables (EEG channels). CGCI is based on vector autoregressive models (VAR).
- In EEG: **many channels** and **small time windows** ➔ VAR estimation unstable. Solution: **restricted VAR models**.
- Optimal VAR restriction (assessed by a simulation study): modified backward-in-time selection method (mBTS) [1]
- mBTS – VAR gives the Granger causality measures:
  time domain: **restricted Granger causality index (RCGCI)** instead of CGCI. [2]
  frequency domain: **restricted generalized partial directed coherence (RGPDC)** instead of GPDC. [3]

B. Definition of Granger causality measures

Let $X_t = \{X_{1,t}, X_{2,t}, \dots, X_{K,t}\}$ $t = 1, \dots, N$: K-dimensional stationary time series

- **Full model for X_j** (including X_i): called **U-model**

$$X_{j,t} = a_{j1,1}X_{1,t-1} + \cdots + a_{j1,p}X_{1,t-p} + \cdots + \boldsymbol{a_{ji,1}X_{i,t-1} + \cdots + a_{ji,p}X_{i,t-p}}$$
$$\dots + a_{jK,1}X_{K,t-1} + \cdots + a_{jK,p}X_{K,t-p} + u_{j,t} \quad u_{j,t}\text{: white noise}$$

p: model order (maximum lag) found by e.g. BIC

- **Model as above but excluding without X_i**: called **R−model**

$$X_{j,t} = b_{j1,1}X_{1,t-1} + \cdots + b_{j1,p}X_{1,t-p} + \dots + b_{jK,1}X_{K,t-1} + \cdots + b_{jK,p}X_{K,t-p} + e_{j,t}$$

$e_{j,t}$: white noise

$$\boldsymbol{CGCI_{X_i \to X_j|Z} = ln(Var(e_{jt}) / Var(u_{jt}))}$$

Z: the other K-2 variables

Fourier transform of coefficients of U-model for X_j

$$A_{ji}(f) = \begin{cases} 1 - \sum_{r=1}^{p} a_{ji}(r)e^{-i2\pi fr}, & if\ i = j \\ -\sum_{r=1}^{p} a_{ji}(r)e^{-i2\pi fr}, & otherwise \end{cases}$$

$$GPDC_{X_i \to X_j|Z}(f) = \frac{\frac{1}{\sigma_{i,i}}|A_{ji}(f)|}{\sqrt{\sum_{k=1}^{K} \frac{1}{\sigma_{k,k}^2} |A_{k,i}(f)|^2}}$$

GPDC is computed at each frequency, f, within an appropriate range of frequencies

C. Definition of restricted Granger causality measures

The set of lagged variables:

$$\{X_{1,t-1}, \dots, X_{1,t-p}, \dots, X_{K,t-1}, \dots, X_{K,t-p}\}$$

mBTS [1]

$\boldsymbol{w_j}$: the subset of the relevant lagged variables for $X_{j,t}$ (the terms of the U-model)

- Check if lagged X_i are present in $\boldsymbol{w_j}$.
- If no ➔ $\mathrm{RCGCI}_{X_i \to X_j}$=0 , $\mathrm{RGPDC}_{X_i \to X_j}$=0
- If yes ➔ compute on the basis of this U-model

  $\mathrm{RCGCI}_{X_i \to X_j}$ and $\mathrm{RGPDC}_{X_i \to X_j}$

Main advantage:
The DR representation involves only a subset of the set of all *Kp* lagged variables and thus it can be applied even in problems where *Kp>N*.

Algorithm mBTS for X_j

Algorithm 1 mBTS for X_j

Require: X: The set of K time series

$w \leftarrow \emptyset$ ▷ initially explanatory vector is empty
$BICold \leftarrow s^2$ ▷ s^2: the error variance
$maxlags \leftarrow [0, \dots, 0]$ ▷ the K maximum lags are initially set to zero
while $sum(maxlags) < Kpmax$ **do**
  for $i = 1 : K$ **do**
    if $maxlags(i) < pmax$ **then**
      $wcand \leftarrow \{w; (i, maxlags(i) + 1)\}$
      $BIC(i) \leftarrow \mathrm{modelfit}(j, X, wcand)$
    else
      $BIC(i) \leftarrow BICold$
  $[BICnew, k] \leftarrow \min(BIC)$ ▷ k is the corresponding index to min
  if $BICnew < BICold$ **then**
    $BICold \leftarrow BICnew$
    $w \leftarrow \{w; (k, maxlags(k) + 1)\}$
    $maxlags(k) \leftarrow maxlags(k) + 1$
  else
    for $i = 1 : K$ **do**
      $maxlags(i) \leftarrow \min(maxlags(i) + 1, pmax)$
return w

D. Electroencephalograms - EEG Data

(*provided by the Laboratory of Clinical Neurophysiology, Medical School, Aristotle University of Thessaloniki, Greece*)

one scalp multi-channel electroencephalographic (EEG) recording of a patient:

- contains 9 episodes of epileptiform discharge (ED)
  ED: interictal ED or subclinical electrographic seizure
- sampling time = 1/1450 sec, downsampled to 1/200 sec
- band-pass filter at [0.3,70] Hz (FIR filter of order 70)
- initially referenced to the right mastoid and re-referenced to infinity (REST, [4])
- channels with artifacts were removed resulting in 28-33 artifact-free channels (depending on episode)
- for each of the 9 episodes, the ED is terminated by the administration of transcranial magnetic stimulation (TMS) (block of 5 TMS at 5 Hz frequency)

E. Application of measures on EEG data

- episodes last ~23 sec (10 sec **preED**, ~3 sec **ED**, 10 sec **postED**)
- overlapping sliding windows of duration of 2 sec, step 1 sec

Computational setting of Granger causality measures

CGCI-RCGCI

- p_{max}=3, *N* =400 (2 sec window)

GPDC-RGPDC

- p_{max}=3, *N* =400 (2 sec window)
- Range of frequencies: 0-50 Hz
- average of GPDC and RGPDC over all frequencies in:
  - delta band (δ) (0-4 Hz)
  - theta band (θ) (4-8 Hz)
  - alpha band (α) (8-16 Hz)
  - beta band (β) (16-35 Hz)
  - gamma band (γ) (32-50 Hz)

Network Brain Connectivity

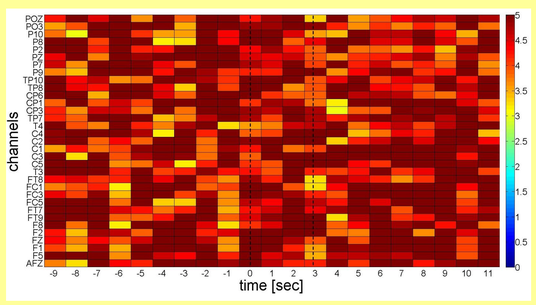
- connectivity of each channel (out-strength of the node of each sliding window) : $s_i = \frac{1}{K-1}\sum_{j=1}^{K} M_{X_i \to X_j}$
  (*M:* CGCI,RCGI,GPDC,RGPDC)
- average strength over all channels: $S = \frac{1}{K}\sum_{i=1}^{K} s_i$

Results

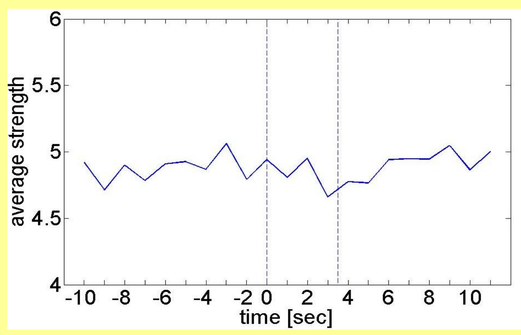
GPDC θ band

preED state | ED state | postED state

s_i for one episode

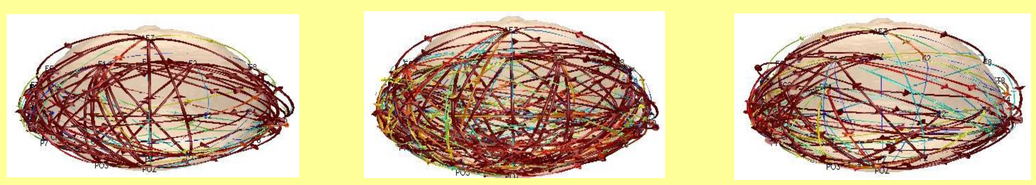


S for one episode

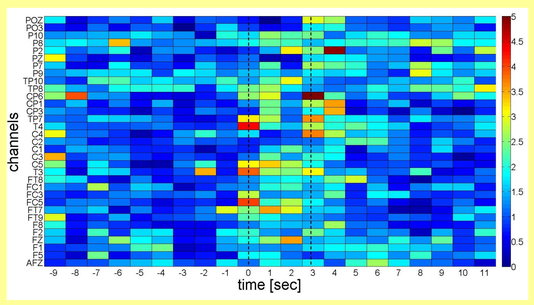


RGPDC θ band

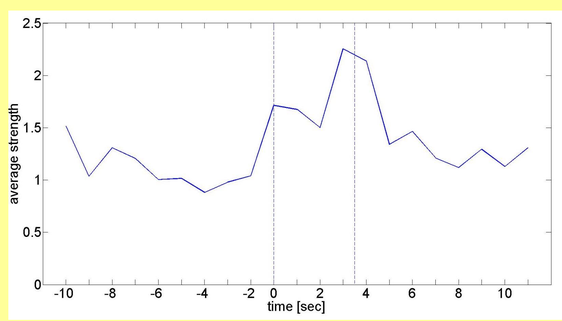
preED state | ED state | postED state



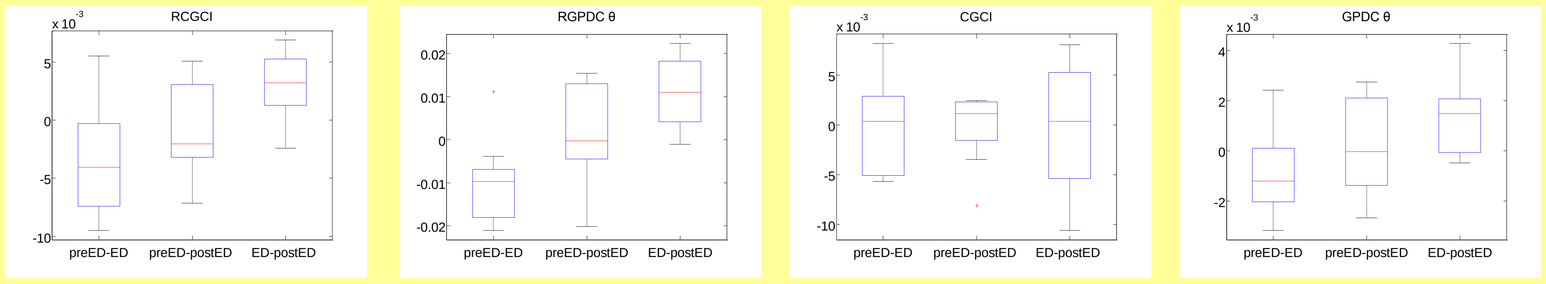
s_i for one episode



S for one episode



Boxplots for the average strength differences for preED-ED, preED-postED and ED-postED from 9 episodes.



p-values for test of mean differences (t-test)

	preED-ED	preED-postED	ED-postED
RCGCI	**0.039** *	0.734	**0.027** *
RGPDC θ band	**0.039** *	0.910	**0.007** *
RGPDC α band	0.074	0.910	0.054
CGCI	0.910	0.734	1
GPDC θ band	0.203	0.734	0.097
GPDC α band	0.734	0.496	0.203

* statistical significant for $\alpha = 0.05$

Conclusions

- The original Granger causality measures, CGCI and GPDC, find little difference in brain connectivity before (preED), at ED (ED) and after ED (postED). They fail to discriminate preED and ED states as well as ED and postED-ED states.
- The Granger causality measures making use of dimension reduction, RCGCI and RGPDC (particularly θ band), show increased brain connectivity during ED. They discriminate the ED state from preED and postED with statistical significance.
- The discrimination of preED vs ED and ED vs postED with RCGCI and RGPDC is consistent with the results on the same data obtained with information based Granger causality measure making use of dimension reduction (PMIME) [5].

References

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