Directed coupling measures for interhemisheric information flow from epileptic EEG

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***Abstract* ð The aim of this work is to evaluate two directed coupling measures in determining interhemisheric information flow from electroencephalograms (EEG) of epileptic patients. In particular, the frontal, central and parietal cortices are considered. The first measure is the directed coherence, a linear measure defined in the frequency domain, and the second the transfer entropy, a nonlinear information measure defined in the time domain. The two measures are computed on consecutive EEG segments from each pair of channels at the different brain areas over a time period that covers the preictal, ictal and postictal state. The profiles of the two measures over the recording period are obtained for 8 extracranial epileptic EEG records, 7 of general tonic clonic type and one of temporal lobe type, all from different patients. Discrimination of the preictal state from postictal state could be established in almost all episodes by transfer entropy and in only few with the directed coherence. The results for the direction of the causal effects were not conclusive as the measures indicated both similar and opposite causal effects.**

*Keywords*ð **epilepsy, EEG, causality, transfer entropy, directed coherence.**

I. INTRODUCTION

The main tool in the study of brain activity prior, on and after epileptic seizures is the electroencephalogram (EEG) recording produced by a number of intra-cranial or extra-cranial channels, which can be seen as a set of time series carrying information about the electric potential at different brain areas. In many studies, brain activity has been assumed to be a complex dynamical system, and measures of interactions and information flow among the components of the system (i.e., brain areas) have been used in the analysis of EEG. In epilepsy, the main interest is to utilize information from measures computed on the preictal EEG record in order to predict impending seizures [1,2]. Though many works concentrate on measures applied to each channel separately (i.e., on the scalar time series), much interest in the recent years is for measures of bivariate and multivariate time series analysis, and especially measures that can detect the direction and strength of the information flow, e.g., see [2,3].

In this study, we analyze EEG records covering preictal, ictal and postictal state and evaluate two measures of directed interaction in their ability to detect changes in the information flow at specific brain areas within the preictal period of up to 3 hours prior to seizure onset, as well as between preictal and postictal periods. The two measures are the directed coherence [4], a standard linear measure derived by the power spectrum and cross-spectrum, and the transfer entropy [5], a nonlinear measure of information flow based on entropies of joint vectors from the driving and the driven system. Both methods have been reported to be able to track changes on the EEG signals, e.g. see [6,7]. There are a number of other directed interaction measures, often referred to as Granger causality or coupling measures, and more recent variants that attempt to detect only the direct effects from one system to the other in the presence of other time systems, as typically is the case with multi-channel EEG, e.g. see [8].

II. METHODOLOGY

A. EEG

We use 8 extra-cranial EEG records from 7 epileptic patients with generalized tonic clonic seizures (denoted as records A, C, D to H) and one with left back temporal lobe epilepsy (denote as record B). A high-pass filter at 0.3Hz and a low-pass filter at 40Hz have been used, and the data were down-sampled to 100 Hz. No other pre-processing or artifact rejection was performed, but in order to attain better source derivation at small cortical regions, for each EEG channel, the mean EEG of the four neighboring channels was subtracted [9]. The two interaction measures were computed on the following pairs of spatially transformed EEG: central left (C3) vs right (C4), temporal left (T7) vs right (T8), frontal left (F3) vs right (F4) and parietal left (P3) vs right (P4). Each EEG record covers at least 3h prior to seizure onset and extends well into the postictal period.

B. Directed interaction measures

Directed coherence (DC) has been introduced in the frequency domain to detect Granger-causal interactions between two systems X on Y measured by the two univariate time series $\{x(t)\}$ and $\{y(t)\}$, t=1,é ,n, respectively. First, the autoregressive model of order P, AR(P), is fitted to the bivariate time series

$$\begin{pmatrix} x(t) \\ y(t) \end{pmatrix} = \sum_{i=1}^{p} \begin{pmatrix} a_{xxi} & a_{xyi} \\ a_{yxi} & a_{yyi} \end{pmatrix} \begin{pmatrix} x(t-i) \\ y(t-i) \end{pmatrix} + \begin{pmatrix} e_x(t) \\ e_y(t) \end{pmatrix} \quad (1)$$

where Ǔ stands for the model coefficients. Input series e_x and e_y consist of common component W_s and independent components W_x and W_y with weighting factors b_{mn}

$$\begin{aligned} e_x(t) &= b_{xx}W_x(t) + b_{xs}W_s(t) \\ e_y(t) &= b_{yy}W_y(t) + b_{ys}W_s(t) \end{aligned} \quad (2)$$

where W_s, W_x and W_y are three white noise sources, mutually independent, with zero mean and variance one. The Fourier transform of AR(P) in Eq. (1) reads

$$\begin{pmatrix} X(f) \\ Y(f) \end{pmatrix} = \quad (3)$$

$$\begin{pmatrix} 1-\sum_i a_{xxi}e^{-jwi\Delta t} & -\sum_i a_{xyi}e^{-jwi\Delta t} \\ -\sum_i a_{yxi}e^{-jwi\Delta t} & 1-\sum_i a_{yyi}e^{-jwi\Delta t} \end{pmatrix}^{-1} \times \begin{pmatrix} b_{xx} & b_{xs} & 0 \\ 0 & b_{ys} & b_{yy} \end{pmatrix} \begin{pmatrix} W_x(f) \\ W_s(f) \\ W_y(f) \end{pmatrix} =$$

$$= \begin{pmatrix} H_{xx}(f) & H_{xs}(f) & H_{xy}(f) \\ H_{yx}(f) & H_{ys}(f) & H_{yy}(f) \end{pmatrix} \times \begin{pmatrix} W_x(f) \\ W_s(f) \\ W_y(f) \end{pmatrix}$$

where $H_{mn}(f)$ denotes the system transfer function from system m to system n. Then DC is defined as

$$DC_{X\to Y}(f) = \frac{H_{xy}(f)}{\sum_{m}^{x,s,y} |H_{xm}(f)|^2} \quad (4)$$

to measure the directed linear influence of X on Y at frequency f. Often the mean value for a range of frequencies is used as the DC measure.

Transfer entropy (TE) from X to Y quantifies the amount of information explained in Y at T time steps ahead from the state of X accounting for the concurrent state of Y. The systems are observed again from univariate time series, but the states of the systems are given in terms of the reconstructed vectors, $\mathbf{x}_t$=(x_t,x_{t-}ǖé ,$x_{t-(m-1)}$ǖ)Njand $\mathbf{y}_t$=(y_t,y_{t-} ǖé ,$y_{t-(m-1)}$ǖ)Nj respectively, where Ű is the delay time and m is the embedding dimension. The use of the same m and Ű for the two systems is typical in applications and was recently found to be the most efficient [8]. TE from X to Y is defined as

$$\begin{aligned} TE_{X\to Y} &= H(\mathbf{x}_t, \mathbf{y}_t) - H(x_{t+T}, \mathbf{x}_t, \mathbf{y}_t) \\ &\quad + H(x_{t+T}, \mathbf{y}_t) - H(\mathbf{y}_t) \end{aligned} \quad (5)$$

where $H(x)$ is the Shannon entropy of the variable X measuring the amount of uncertainty associated with the values x of X, and for a discrete variable is defined as

$$H(X) = -\sum p_X(x)\log p_X(x), \quad (6)$$

where p_X(x) is the probability mass function of X. Here, we estimate entropies using the k-nearest neighbor estimating method in [11].

C. Set Up

The measures DC and TE are calculated in both directions (XŸ Y and YŸ X) on non-overlapping consecutive EEG segments of 30s for the four channel pairs from each of the 8 records. For the estimation of DC, three orders of AR are tested, P =3,6,10, and DC was averaged over frequencies from 1 to 30 Hz with step 1 Hz. The embedding dimension m for TE is the analogous parameter to P for DC, and therefore we use also m = 3,6,10. The other parameters of TE are Ű=1 and T=1.

D. RESULTS

We obtained one measure profile from the computation of the measure on consecutive segments covering the whole record, from the preictal to the postictal state, for each channel pair and direction of interaction. The profiles from both measures vary with the epileptic episode and the channel pair. The profiles of DC (P=10) are shown in Fig.1 for all channel pairs and three representative episodes, and the TE (m=10) profiles for the respective data are shown in Fig.2. There are variations within the preictal periods, as observed by both DC and TE profiles, but not in any consistent manner that would indicate a persistent change, say from early to late preictal state.

The overall DC profiles do not indicate any change from preictal to ictal and postictal states, whereas TE profiles show clearly this transition for almost all pairs, episodes and coupling directions. For example, this can be clearly seen in record B (second panel of Fig.1 for DC and Fig.2 for TE), where the postictal period is longer than for the other episodes, and TE is at a higher level during the postictal period for all channel pairs and directions, whereas for DC this can be seen only for the case F4$\to$F3.

The selection of the order P in the estimation of DC does not seem to affect significantly the performance of the measure. Even for larger values of P that we tested (up to P=30), the main signatures of the profiles are intact. On the other hand, TE seems to be more dependent on the embedding dimension m, and in particular the transition from preictal to ictal and postictal is more obvious for m=10.

Both measures give mostly positive values in both directions and along all states, indicating that bidirectional causal effects are persistent between brain areas at the two hemispheres. Even for the cases where one measure gives significantly larger causal effect in the one direction, often the other measure suggests a larger effect in the opposite direction, e.g. DC shows larger effect from C3 to C4 in episode

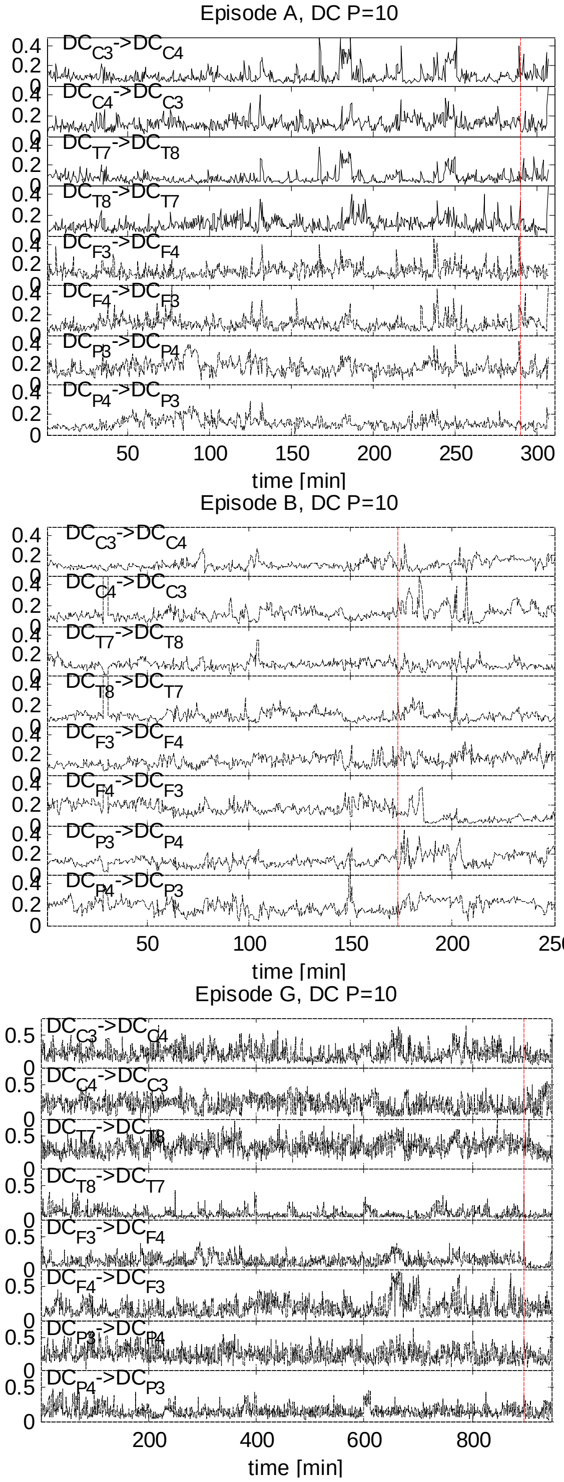

Figure 1 DC (P=10) profiles for records A, B and G, (preictal, ictal and postictal states) and all channel pairs, as denoted at each subplot. The red dashed vertical line denotes seizure onset.

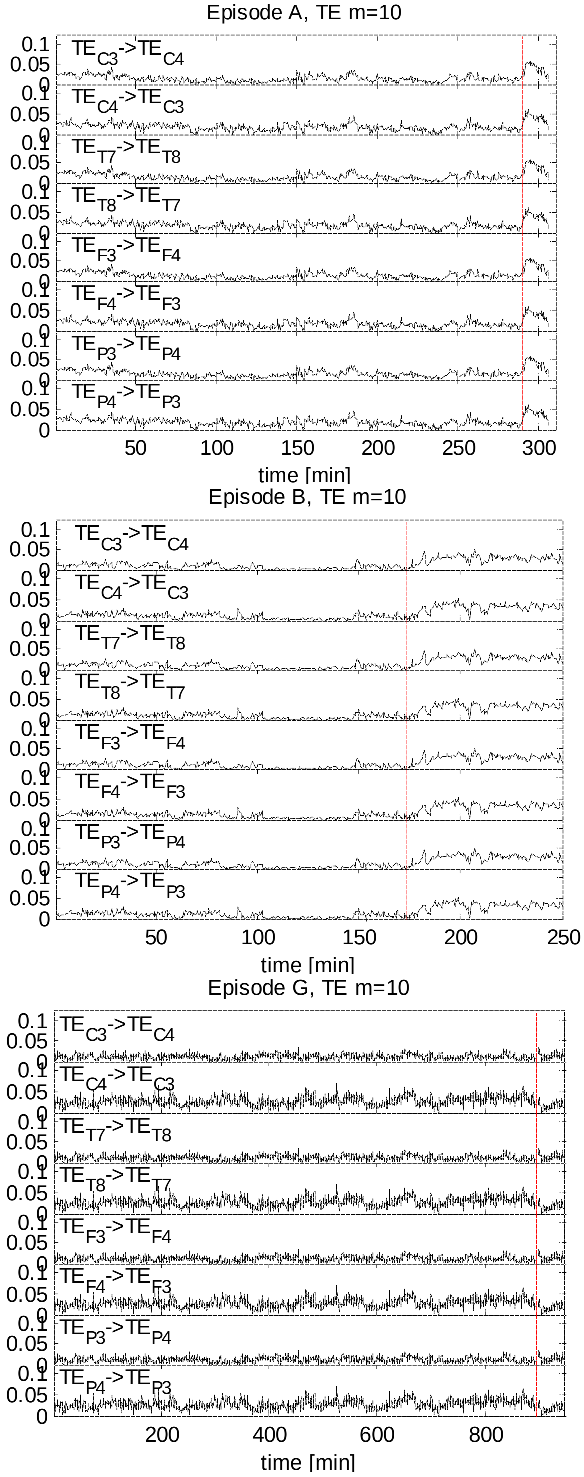

Figure 2 As Fig.1 but for TE (m=10).

G (third panel of Fig.1), whereas TE shows larger effect from C4 to C3 for the same episode (third panel of Fig.2). For the same record, DC indicates a clear driving of T7 on T8 at the preictal state, while the opposite is observed with TE. Moreover, DC distinguishes preictal and postictal states only for certain channel pairs, i.e., DC values increase for C4→C3 (driving from right to left hemisphere) and decrease for T7→T8 and F3→F4 (driving from left to right hemisphere). TE detects for all pairs the transition of preictal to ictal and postictal state, and indicates a decrease of information flow independently of the direction. Again these results do not indicate a particular tendency of driving from one hemisphere to the other.

TE values are slightly larger than zero at almost all cases, e.g. for record A the estimated values of TE (m=10) from both directions are around 0.02. DC gives larger values than TE at almost all cases (the scale of values of DC and TE in the figures is different), e.g. for record A the estimated values of DC (P=10) from both directions are around 0.12. Though the DC and TE measures are not normalized to an easily interpretable scale, TE tends to be less significant. For both measures it is necessary to assess statistical significance, i.e., whether small measure values suggest no connectivity rather than small interaction, in order to correctly interpret the results in terms of connectivity of brain areas. Some work on the use of surrogates for assessing statistical significance of coupling measures has been done recently [12,13], and we also work on developing measures with improved statistical significance.

III. CONCLUSIONS

Both the directed coherence (DC) and transfer entropy (TE) measures seem to vary much across the episodes, the channels and the states. The positive values of both measures at almost all cases (episodes, channels) suggest the existence of bidirectional causal effects among the different brain areas, and thus the interaction of the two hemispheres, however further investigation should be assessed to validate the statistical significance of the measures. TE increases after the seizure onset at almost all epileptic episodes (apart from episode G, where there is first a drop and then an increase), indicating the increase of information flow among the brain areas. This can possibly be attributed to the decrease of complexity in the brain dynamics during the seizure, but it can as well be an artificial feature, e.g. the more rhythmic oscillations on seizure and at a lesser extend during the postictal state may give rise to an increase of the coupling. Both measures seem to be insufficient in detecting a precursor of the seizure onset, as no changes in the information flow are detected just before the seizure onset. As EEG data are multidimensional, the need of measures that quantify the overall causal effects and differentiate among direct and indirect causal effects is imperative.

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