Evidence of self-organization in brain electrical activity using wavelet-based informational tools

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Abstract

In the present work, we show that appropriate information-theory tools based on the wavelet transform (relative wavelet energy; normalized total wavelet entropy, $H$; generalized wavelet complexity, $C_W$), when applied to tonic–clonic epileptic EEG data, provide one with valuable insights into the dynamics of neural activity. Twenty tonic–clonic secondary generalized epileptic records pertaining to eight patients have been analyzed. If the electromyographic activity is excluded the difference between the ictal and pre-ictal mean entropic values ($\Delta H = \langle H^{\text{ictal}} \rangle - \langle H^{\text{pre-ictal}} \rangle$) is negative in 95% of the cases ($p < 0.0001$), and the mean complexity variation ($\Delta C_W = \langle C_W^{\text{ictal}} \rangle - \langle C_W^{\text{pre-ictal}} \rangle$) is positive in 85% of the cases ($p = 0.0002$). Thus during the seizure entropy diminishes while complexity grows. This is construed as evidence supporting the conjecture that an epileptic focus in this kind of seizures triggers a self-organized brain state characterized by both order and maximal complexity.

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1. Introduction

In the characterization of the time evolution of the complex EEG dynamics, quantifiers based on nonlinear dynamics have been applied by investigating: (i) the temporal evolution of the EEG signal’s correlation dimension $D_2$ and, (ii) the associated degree of chaoticity (largest Lyapunov exponent, $A_{\text{max}}$). A transition from a rather complex behavior (of the neural network) to a much simpler one can be detected at (or just before) epileptic seizure onset [1,2]. Despite the obvious physiological relevance of such findings, serious doubts arise concerning the applicability of nonlinear metric tools to this endeavor. EEG-time series should be representative of a unique and stable attractor (i.e., be stationary) for nonlinear dynamic metric tools to be applicable. This is not the case with EEGs. Application of deterministic chaos’ ideas to EEG data remains highly controversial. The concomitant interpretation of data is still under discussion [3]. An alternative, natural approach for quantifying the degree of order of a complex signal is provided by its spectral entropy (SE), as defined from the Fourier power spectrum [4]. The SE measures just how “concentrated” the Fourier power spectrum of a signal is. However, the Fourier transform (FT) requires stationarity of the concomitant signal and EEGs are highly nonstationary. The terms “nonstationary” and “time varying” mean that the statistical properties, which are the statistical moments, change with time. Statistical tests of stationarity EEG time series have revealed a variety of results depending on conditions, which estimate the amount of time during which the EEG is stationary, ranging from several seconds to several minutes [5–8]. In the case of tonic–clonic EEG records stationarity of the time series can be assumed for intervals of 30 s [9,10]. However, as a practical matter, whether or not a data segment is considered stationary depends on the problem being studied, the type of analysis being performed, and the measure used to characterize the data. Moreover, the FT does not yield the time evolution of the frequency patterns associated to the traditional EEG bands ($\delta: 0.5–3.5 \text{ Hz}; \ \theta: 3.5–7.5 \text{ Hz}; \ \alpha: 7.5–12.5 \text{ Hz}; \ \beta: 12.5–30.0 \text{ Hz}; \ \gamma: > 30.0 \text{ Hz}$) [11,12]. As a consequence, the spectral entropy does not get defined as a function of time.

All the above difficulties can be overcome by using the wavelet transform [13–15], an efficient time–frequency decomposition method. In particular, the orthogonal discrete wavelet transform (ODWT) makes no assumptions about a record’s stationarity. The only input needed is the time series itself. If the Shannon entropy is computed via the wavelet transform, the time evolution of frequency patterns can be followed with an optimal time–frequency resolution. The ensuing entropy-form, i.e., the “normalized total wavelet entropy” (NTWS), carries information about the degree of order/disorder associated with a multi-frequency signal response [14]. Consequently, the time evolution of the NTWS would yield information concerning the dynamics associated with the EEG records [9,16–18].

Our goal here is to introduce the notion of *complexity* within such a wavelet scenario so as to gather new insight into the dynamical transition from epileptic tonic and clonic stages. Definitions of complexity can be classified into three groups, according to the calculational procedure one employs [19–21]: (i) computational
complexity, based on algorithms or automata, useful for symbolic dynamics or chaotic maps and very difficult to calculate, (ii) complexities based on the measure of the entropy, useful for dealing with nonequilibrium systems. They are either difficult to calculate or have a very simple relation to entropy, and/or (iii) complexities calculated from probability distributions, but independent of the entropy. Here we will work with the last procedure.

López-Ruiz, Mancini, and Calbet (LMC) have proposed a measure of complexity based on the notion of “disequilibrium” [19,20]. The notion of statistical complexity advanced by LMC constitutes an important step towards building up an armory of measures that are both easy to compute and to intuitively grasp. It exhibits, nonetheless, some difficulties that have been lucidly pointed out in, for instance, Refs. [22,23]. As a further step in the direction put forward by López-Ruiz, Mancini, and Calbet, we recently called attention to the mind-opening study of Wootters’ [24] regarding the notion of distance in probability spaces. Following the suggestions of Wootters’ [24], we have revisited the LMC statistical complexity measure and replaced their definition of disequilibrium by one that incorporates, instead of the Euclidean disequilibrium, the Wootters’ one. In this way, a generalized LMC measure of statistical complexity was introduced [25]. With the help of both the normalized total wavelet entropy (NTWS) and the generalized LMC wavelet complexity notion we will detect the presence of a rather special brain-state characterized by both order and large complexity. Now, the brain’s electrical activity (“seen” by EEGs) can be associated to a chaotic dynamics (see Refs. [2,3,9]). The coexistence of these characteristics is, according to Haken, the signature of “self-organization” [26,27]. Thus, some of the brain’s neurons would acquire spatial, or spatio-temporal structures by means of internal processes, without specific interference from the outside.

2. Subjects and data recording

Twenty secondary generalized tonic–clonic epileptic seizures (TCES) from eight epileptic patients admitted for video-EEG monitoring were analyzed [28]. The patient group consisted of four males and four females, age 30.87 ± 15.27 (mean ± SD; range 6–51), with a diagnosis of pharmaco-resistant epilepsy and no other accompanying disorders. Clinical data are presented in Table 1. Scalp electrodes (F1, F2, F7, F3, F4, F8, T3, C3, C4, T4, T5, P3, Pz, P4, T6, O1, O2) with bimastoideal reference were applied following the 10–20 international system. Each signal was digitized at 409.6 Hz through a 12-bit A/D converter and filtered with an “antialiasing” 8 pole low-pass Bessel filter, with a cutoff frequency of 50 Hz. Then, the signal was digitally filtered with a 1–50 Hz bandpass filter (bi-directional with zero phase) (physician frequency range of interest for diagnosis) and stored, after decimation, at $\omega_s = 102.4$ Hz (sample frequency) in a PC hard drive.

Recordings were done under video control to have an accurate determination of the different stages of the seizure. The different stages of EEG signals (pre-ictal, seizure start, tonic phase, clonic phase, seizure end, post-ictal) were determined by
the physician team. In the cases where it was impossible to trace a clear frontier between tonic and clonic phases, a transition interval was marked by the physician team. Off-line analysis was performed with characterization of semiological features, timing of the onset and definition, when possible, of the anatomical focus for each event (see Table 1). Analysis for each event included 60 s of EEG before the seizure onset and 120 s of ictal and post-ictal phases. All 180 s were analyzed at the right central region, C4 derivation; this electrode has been chosen after visual inspection of the EEG, by the physician team, as the one with the least number of artifacts. The time intervals of the pre-ictal stage which present artifacts (ocular and other movements, etc.) were marked by the physician team and were excluded in the subsequent analysis.

A scalp EEG signal is essentially a nonstationary time series that presents artifacts due mainly to muscle activity as measured by an electromyogram, among others, that are especially troublesome in the case of tonic–clonic epileptic seizures, where they reach very high amplitudes contaminating the seizure recording. Gastaut and Broughton [29] described a characteristic frequency pattern during a tonic–clonic epileptic seizure in patients subjected to muscle relaxation from curarization and artificial respiration. After a short period characterized by a desynchronization phase they detected an “epileptic recruiting rhythm” at about 10 Hz and later, as the seizure ends, a progressive increase of the lower frequencies associated with the

<table>
<thead>
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<th>Patient</th>
<th>Edge (years)</th>
<th>Sex</th>
<th>Seizure Number</th>
<th>Start (s)</th>
<th>End (s)</th>
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The start and end of the seizure is (in seconds) referring the origin to the beginning of the records.
clonic phase. About 10 s after the seizure onset, lower frequencies (0.5–3.5 Hz) were observed that gradually descend their activity. The clonic activity is associated to generalized polyspike bursts at each myoclonic jerk. Very slow irregular activity then dominates the EEG, accompanied by a gradual frequency increase of up to (3.5–12.5 Hz), indicative of the end of the seizure.

As an example, in Fig. 1 we present a scalp EEG signal (second seizure of patient B, see Table 1) corresponding to a TCES recorded over C4 channel. In this record, the pre-ictal phase is characterized by amplitude signal /C24 50 mV:

The seizure starts at 74 s, with a discharge of slow waves superimposed with low-voltage fast activity. This discharge lasted approximately 11 s and with a mean amplitude of 100 mV. In Fig. 1, one can easily note the low waves in the first 4 s in the frequency range 2–4 Hz, but for the remaining 7 s it is not so evident. For a more accurate description of this period see Fig. 2 and the corresponding discussion in Section 4. Afterwards, taking into account the behavior in all electrodes, the seizure spreads, making the analysis of the EEG more complicated due to muscle artifacts. It is possible, however, to establish the beginning of the clonic phase at approximately 120 s and the end of the seizure at 158 s when there is an abrupt decay of the signal amplitude.

3. Wavelet analysis

3.1. Wavelet energy and wavelet entropy

Wavelet analysis relies on the use of (i) an appropriate basis and (ii) a characterization of the signal by the amplitude-distribution in such a basis [30,31]. The wavelet coefficients efficiently provide both full information and a direct estimation of local energies at the different scales [13–15,9,16–18].

Our EEG signal is assumed to be given by the sampled values $\mathcal{S} = \{s_0(k); k = 1,\ldots,M\}$, corresponding to a uniform time grid. If the discrete diadic wavelet decomposition is carried out over all resolutions levels, $j = -N_0,\ldots,-1$ ($N_0 = \log_2(M)$, with $M$ the number samples) the wavelet expansion reads

$$\mathcal{S}(t) = \sum_{j=-N_0}^{-1} \sum_k C_j(k) \psi_{j,k}(t) = \sum_{j=-N_0}^{-1} r_j(t),$$

where $\psi_{j,k}(t) = 2^{j/2} \psi(2^j t - k)$ with $j, k \in \mathbb{Z}$ and $\psi(t)$ the mother wavelet, $k$ is the time index and at each wavelet resolution level $j$ one has $N_j = 2^j M$ coefficients. The wavelet coefficients $C_j(k)$ can be interpreted as the local residual errors between successive signal approximations at scales $j$ and $j + 1$ [30,31]. The above expansion yields information on the signal $\mathcal{S}(t)$ pertaining to the frequencies $2^{-1} \omega_s \leq |\omega| \leq 2^j \omega_s$.

If the family $\{\psi_{j,k}(t)\}$ is an orthonormal basis for $L^2(\mathbb{R})$, the concept of energy is linked with the usual notions derived from Fourier’s theory. The wavelet coefficients are given by $C_j(k) = \langle \mathcal{S}, \psi_{j,k} \rangle$ and the energy, at each resolution level $j = \ldots,
Fig. 1. Scalp EEG signal for a generalized epileptic tonic–clonic seizure, recorded at central right location (C4). The seizure starts at 74 s and ends at 158 s. Notice that, visually, the dramatic transition from rigidity (tonic stage) to convulsions (clonic stage) around 120 s is not clearly discernible.
The total energy can be obtained in the fashion

$$E_{\text{tot}} = \| \mathcal{S} \|^2 = \sum_{j=-N_0}^{-1} \sum_k |C_j(k)|^2 = \sum_{j=-N_0}^{-1} E_j.$$  \hfill (3)

Finally, we define the normalized $\rho_j$-values, which represent the relative wavelet energy (RWE)

$$\rho_j = E_j / E_{\text{tot}}$$  \hfill (4)

for the resolution levels $j = -N_0, \ldots, -1$. The RWE, $\rho_j$, yield at different scales the probability distribution for the energy. Clearly, $\sum_{j=-N_0}^{-1} \rho_j = 1$ and the distribution $\{\rho_j; \ j = -N_0, \ldots, -1\}$ can be considered as a time-scale density that constitutes a suitable tool for detecting and characterizing specific phenomena in both the time and the frequency planes [14,15,9,16–18].

Shannon’s information measure gives a criterion for analyzing and comparing probability distributions. It measures the informative content of any distribution.
We define the normalized total wavelet entropy (NTWS) as

\[ H = - \sum_{j=-N_0}^{N_0} \rho_j \ln[\rho_j]/\ln[N_0]. \] (5)

The NTWS is a measure of the degree of order/disorder of the signal and provides useful information about the underlying dynamical process associated with the signal [9]. Indeed, a very ordered process can be represented by a periodic monofrequency signal (signal with a narrow band spectrum). A wavelet representation of such a signal will be resolved at one unique wavelet resolution level, i.e., all relative wavelet energies will be (almost) zero except at the wavelet resolution level which includes the representative signal’s frequency. For this special level the relative wavelet energy will (in our chosen energy units) almost equal unity. As a consequence, the NTWS will acquire a very small, vanishing value. A signal generated by a totally random or chaotic process can be taken as the representative of a very disordered behavior. This kind of signal will have a wavelet representation with significant contributions coming from all frequency bands. Moreover, one could expect that all contributions will be of the same order. Consequently, the relative wavelet energy will be almost equal at all resolutions levels, and the NTWS will acquire its maximum possible value. The NTWS appears as a measure of the degree of order/disorder of the signal. Thus, it can provide useful information about the underlying dynamical processes associated with the signal [9].

3.2. Wavelet transforms and signal separation

Natural phenomena produce time series that, usually, contain, in addition to the desired “clean” signal, (i) effects of contamination by the environment through which the signal passes on its way from the source to the measurement device, or (ii) contamination by properties of the measurement process itself. In many applications one wishes for a separation between signal and noise. The elimination of the high-frequency muscle activity present in the TCES (in the frequency range given by frequency bands \( B_1 \) and \( B_2 \); see Section 4) with the use of traditional filters has some disadvantages [32–34]: (a) filtering frequencies related to muscle artifacts also affect the morphology of the remaining ones and, (b) the filtering process alters the nonlinear metric invariants. In order to overcome the above limitations a signal separation based on orthonormal wavelets was used. When noise (signal contamination) is present only in specific frequency bands, a filtering process or signal separation (assuming additively between signal and noise) based on an orthonormal wavelet transform can be efficiently implemented. Supposing, as in the case of TCES, that we are interested in eliminating high-frequency noise. Using Eq. (1) at a \( j_0 \)-scale we can obtain a smoothed version of the original signal by recourse to

\[ \tilde{S}(t) = \sum_{j=-N_0}^{j_0} r_j(t). \] (6)
This smoothed signal has a lesser amount of high frequencies as compared to the \( j_0 + 1 \)-level, but it will possess just half the number of data than that of the previous level. The original sample ratio can be obtained by a cubic spline interpolation.

One of the main reasons for employing a signal separation method based on orthogonal wavelets lies in the fact that it enables one to analyze the “de-noised” signal without seriously impairing the interpretation of the associated dynamics. Mallat [31] proved that, for a one-dimensional signal denoising process (assuming additive noise), an orthogonal wavelet-based method is better than a method based on Fourier Transforms, because wavelets do not change the original signal. The main advantage of filtering, or signal separation, with orthonormal wavelets, lies in the fact that (i) the morphology of the nonfiltered frequencies is not affected, and, therefore, the dynamics associated with those nonfiltered frequencies does not change either, (ii) as a consequence, easy implementation of the technique becomes feasible. In evaluating quantifiers based on wavelet-coefficients, one needs only to consider that the contribution of frequency bands one wishes to disregard effectively disappears, and not include them in the computation procedure.

3.3. Wavelets complexity

It is important to note that entropy-growth is not tantamount to complexity growth (or vice versa). Periodic motion (zero entropy) is as devoid of complexity as white noise (maximum entropy). Their complexity is null. Statistical complexity (SC) has to do with intricate structures hidden in the dynamics, emerging from a system which itself is much simpler than its dynamics [35]. SC is characterized by the paradoxical situation of complicated dynamics for simple systems. Of course, if the system itself is already complicated enough and contains many different constituent parts, it is obvious that it may support a rather complicated dynamics, but perhaps without the emergence of nitid and typical characteristic patterns [35]. We will use the statistical complexity measure functional form defined by LMC in Refs. [19,20], that reads

\[
C = H \cdot Q,
\]

where \( H \) is the normalized information measure and \( Q \) stands for the so-called “disequilibrium”.

In our case, the normalized information measure is represented by the NTWS \( 0 \leq H \leq 1 \). The disequilibrium \( Q \) is a “distance” in probability space, from our \( \{p_i, i = 1, \ldots, N\} \) to the uniform distribution \( \{p_e = 1/N\} \). LMC proposed the Euclidean distance for a measure of \( Q \). Then

\[
Q_E = Q_0^{(E)} \sum_{i=1}^{N} \left( p_i - \frac{1}{N} \right)^2,
\]

with \( Q_0^{(E)} = N/(N - 1) \) so that \( 0 \leq Q_E \leq 1 \) and the original LMC statistical complexity is given by

\[
C_E = H \cdot Q_E.
\]
The use of Euclidean norm as a definition of distance in a probability space \( \Omega \subset \mathbb{R}^N \) has been criticized by Wootters in an illuminating communication [24]. Essentially, the Euclidean norm ignores the stochastic nature of the distribution \( \{p_i\} \). Thus, following Wootters’ pioneer essay, we redefine the notion of disequilibrium and recast it à la Wootters. Then, the generalized LMC statistical complexity reads [25]:

\[
C_W = H \cdot Q_W ,
\]

where we rewrite the disequilibrium \( Q \) on the basis of a statistical distance specifically designed for a probability space

\[
Q_W = Q_0^{(W)} \cos^{-1} \left\{ \sum_{i=1}^{N} [p_i]^{1/2} \left[ \frac{1}{N} \right]^{1/2} \right\}
\]

with \( Q_0^{(W)} = 1/\cos^{-1}(1/N)^{1/2} \) and \( 0 \leq Q_W \leq 1 \).

Application of the ensuing statistical complexity measure to the logistic map shows that important improvements are thereby achieved. The new measure does behave in a manner compatible with that of the Lyapunov exponents, while the LMC one does not [25].

The LMC complexities (original and generalized) are not trivial functions of the entropy, in the sense that, for a given entropic-value, a whole range of complexities exist, between a minimal \( C_{\text{min}} \) and a maximal value \( C_{\text{max}} \) [36]. Thus, evaluating the complexity provides one with important additional information regarding the peculiarities of a probability distribution. Here we take \( \{p_i; i = 1, \ldots, N\} \) as a probabilistic wavelet energy distribution \( \{\rho_j; j = -N_0, \ldots, -1\} \) and \( N = N_0 \) the number of states. Since the generalized LMC complexity is derived from the wavelet treatment of a time series, we call it a wavelet statistical complexity.

### 3.4. Wavelet quantifiers time evolution

Since we are mainly interested in the time-evolution of brain signals, we divide up a given such signal into non-overlapping temporal windows of length \( L_w \) and, for each interval \( i (i = 1, \ldots, N_T) \), with \( N_T = M/L_w \), we evaluate the three quantifiers: RWE, NTWS, and generalized LMC wavelet statistical complexity, \( C_W \). In the case of a dyadic wavelet decomposition, the number of wavelet coefficients at resolution level \( j \) is two times smaller than at the previous, \( j + 1 \), one. The minimum length of the temporal window will therefore include at least one wavelet coefficient in each scale.

The wavelet energy at resolution level \( j = -N_0, \ldots, -1 \) for the time window \( i \) is given by

\[
E_j^{(i)} = \sum_{k=(i-1)L_w+1}^{iL_w} |C_j(k)|^2 \quad \text{with} \quad i = 1, \ldots, N_T ,
\]
while the total energy in this time window will be

$$E_{tot}^{(i)} = \sum_{j=-N_0}^{-1} E_j^{(i)}.$$  \hfill (13)

The time evolution of RWE, NTWS and wavelet complexity $C_W$ will be given by

$$\rho_j^{(i)} = E_j^{(i)}/E_{tot}^{(i)},$$

$$H^{(i)} = -\sum_{j=-N_0}^{-1} \rho_j^{(i)} \ln[\rho_j^{(i)}]/\ln[N_0]$$

and

$$C_W^{(i)} = H^{(i)} \cdot Q_W^{(i)}$$

with

$$Q_W^{(i)} = Q_0^{(W)} \cos^{-1}\left\{ \sum_{j=-N_0}^{-1} \left[ \rho_j^{(i)} \right]^{1/2} \left[ \frac{1}{N_0} \right]^{1/2} \right\}.$$  \hfill (17)

In order to study the time evolution of the complexity, a diagram of $C$ versus time $t$ can then be used. But, as we know, the second law of thermodynamics states that entropy grows monotonically with time ($dH/dt \geq 0$). This implies that $H$ is an arrow of time, so that an equivalent way to study the time evolution of the complexity is to plot $C$ versus $H$. In this way, the normalized entropy substitutes the time axis. LMC have shown that for an isolated system evolving in time its complexity measure cannot attain any arbitrary value in a $C_E$ versus $H$ map. The same is satisfied for $C_W$. Then the complexity $C$ must always stay within certain bounds $C_{min}$ and $C_{max}$. These are the maximum and minimum possible values of $C$, given $H$. A procedure for the evaluation of these two curves, for a given value of $N_0$, is given in Ref. [20] in the case of original complexity $C_E$ and for the generalized complexity in Ref. [36].

4. Results and discussion

In the present study, an orthogonal decimated discrete wavelet transform was applied, in which orthogonal cubic spline functions were used as mother wavelets, $\psi$, and the time–frequency information was organized in a hierarchical scheme [30,31]. Among several alternatives, cubic spline functions were used. They are symmetric, orthogonal, and combine smoothness with numerical advantages in suitable proportions [37,38].

We define six frequency bands for an appropriate wavelet analysis within the multiresolution scheme to be used here, denoted by $B_j$ ($j=1, \ldots, 6$). In Table 2 the boundary frequencies associated with the different wavelet resolution levels $j$ are given according to the signal sample frequency $\omega_s = 102.4$ Hz. Also, in the same table, the relations of these frequency bands to the traditional EEG bands [12] are
given. One must note that due to acquisition data setup (band pass filter 1–50 Hz):
(a) we set \( N_0 = 6 \) and, (b) the effective upper frequency limit for the \( B_1 \) band is 50 Hz and the lower frequency limit for the \( B_6 \) band is 1 Hz.

Our goal is characterize the TCES throughout the time evolution of the three wavelet quantifiers (RWE, NTWS, and generalized LMC statistical wavelet complexity). For this purpose the EEG signal and the corresponding wavelet coefficients series are divided into nonoverlapping epochs of length \( L_w = 1.25 \text{s} \equiv 128 \text{ samples} \) each. In this way, the results obtained will be compatible with our previous works [9,16–18]. If all frequency bands are included in the evaluation of wavelet quantifiers, we must set \( N = 6 \) and \( j = -6, \ldots, -1 \) in the equations of Section 3.4. We ignore the contributions from \( B_1 \) and \( B_2 \) bands at wavelet resolution levels \( j = -1 \) and \( -2 \) (see Table 2), that contain the high-frequency artifacts (muscle activity) that blur the EEG. Although high-frequency brain activity is thereby not considered, its contributions during the ictal stage are not as strong as it is for middle and low frequencies. This has been conclusively demonstrated in Refs. [18,28,29]. Once the high-frequency artifacts are eliminated, we can analyze the time evolution of the above-listed three wavelet quantifiers for the “remaining” signal. In this case we have \( N = 4 \) and \( j = -6, \ldots, -3 \) in the equations of Section 3.4.

An interesting point to note is that although the grouping in frequency bands implies a loss of frequency resolution, it can be more useful than a study of single frequencies or peaks, due to the relations between frequency bands and functions or sources in the brain. In this context, the relative wavelet energy allows for an easy interpretation of several minutes of frequency variations in a single display, something that is sometimes difficult to achieve with traditional scalp EEGs. Fig. 2 displays the RWE (corresponding to the EEG signal shown in Fig. 1) without electromyographic contributions (we “keep” \( B_3–B_6 \)). We see that the pre-ictal phase is characterized by a dominance of low rhythms (pre-ictal: \( [B_3 + B_6] \sim 50\% \)). The seizure starts at 74 s with a discharge of slow waves superimposed to low-voltage fast activity. This discharge lasts approximately 11 s and produces a marked “activity-rise” in the frequency bands \( B_3 \) and \( B_6 \), which reaches 85% of the RWE. Starting at

### Table 2

<table>
<thead>
<tr>
<th>Notation</th>
<th>Wavelet band</th>
<th>EEG band</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \omega_{\text{min}} )</td>
<td>( \omega_{\text{max}} )</td>
</tr>
<tr>
<td>( B_1 )</td>
<td>25.6</td>
<td>51.2</td>
</tr>
<tr>
<td>( B_2 )</td>
<td>12.8</td>
<td>25.6</td>
</tr>
<tr>
<td>( B_3 )</td>
<td>6.4</td>
<td>12.8</td>
</tr>
<tr>
<td>( B_4 )</td>
<td>3.2</td>
<td>6.4</td>
</tr>
<tr>
<td>( B_5 )</td>
<td>1.6</td>
<td>3.2</td>
</tr>
<tr>
<td>( B_6 )</td>
<td>0.8</td>
<td>1.6</td>
</tr>
</tbody>
</table>

The EEG frequency bands correspond to the following frequencies: \( \delta (0.5–3.5 \text{Hz}); \theta (3.5–7.5 \text{Hz}); \alpha (7.5–12.5 \text{Hz}); \beta (12.5–30.0 \text{Hz}); \gamma (> 30.0 \text{Hz}) \).
85 s, the low-frequency activity, represented in our analysis by $B_5$ and $B_6$, decreases abruptly to relative values lower than 10% and 5%, respectively, while the other frequency bands become more important. We also observe in Fig. 2 that the start of the clonic phase is correlated with increased activity in the $B_4$ frequency band. After 140 s, when clonic discharges become intermittent, the $B_5$ activity rises up again till the end of the seizure, when the $B_6$ frequency activity also increases in a very rapid fashion and both frequency bands become clearly dominant. The $B_5$ and $B_6$ frequency bands maintain this predominance throughout the post-ictal phase. Similar results were obtained in 20 tonic–clonic epileptic EEG time series recorded at C4 position, corresponding to 8 different patients. We conclude, from this example and for similar analysis done on the other TCES [18], that the seizure was dominated by the middle frequency bands $B_3$ and $B_4$ (12.8–3.2 Hz), with a corresponding abrupt activity decrease in the low-frequency bands $B_5$ and $B_6$ (3.2–0.8 Hz). Clearly, this behavior can be associated with the epileptic “recruiting rhythm” [29].

A quantification of the epileptic recruiting rhythm based on RWE was made in Ref. [18]. We emphasize the fact that our results were obtained with scalp recordings and without the use of curare or traditional filtering method based on Fourier transform.

The ensuing NTWS (corresponding to the EEG signal shown in Fig. 1), as a function of time, is depicted in Fig. 3. The dashed line represents the time evolution of the NTWS (all frequency bands are included), while the continuous line corresponds to results which ignore contributions due to high-frequency bands ($B_1$ and $B_2$). It is interesting to observe the behavior of the NTWS during the first 11 s following the seizure onset. We see that in this time interval the NTWS exhibits increasing values if all wavelet frequency bands are included. Comparison is to be made with NTWS values in the pre-ictal stage.

![Normalized total wavelet entropy (NTWS) time evolution. The dashed and the continuous lines represent the NTWS time evolution with and without, respectively, the contribution of the frequency bands $B_1$ and $B_2$ (muscular activity). The vertical lines represent the start and end of the epileptic seizure.](image-url)
If the wavelet frequency bands $B_1$ and $B_2$ (bands that contain mainly the muscular activity) are not included, the largest NTWS value is lower than that for the ictal onset. Thus, the behavior of the NTWS following the seizure onset is compatible with an increase in the degree of disorder of the system induced by a high-frequency activity. Super-imposed low- and medium-frequency activities, however, are responsible for the “remaining-signal’s” more ordered behavior. The NTWS behavior after 85 s (in both cases, with and without inclusion of high-frequency bands) is indicative of the fact that the system exhibits a tendency to be more “ordered”. This tendency is better appreciated without muscle activity. Moreover, note that the NTWS in the last case adopts a minimum value around 120 s, in coincidence with the beginning of the clonic phase. The peak observed in the NTWS at $\sim 140$ s could be associated with the disappearance of the epileptic recruitment rhythm. After this point, the NTWS displays increasing values until 158 s, which is defined as the seizure ending time. We see that the NTWS for the post-ictal stage displays almost constant values, comparable to those obtained for the pre-ictal stage. Similar results were obtained for the other TCES signals recorded at C4 position. Summing up, one can associate a more robust degree of order to the EEG activity during the ictal than during the pre- and post-ictal stages [18], compatible with a dynamic process of spatial synchronization (frequency tuning) in the brain activity, since a single EEG electrode placed on the scalp records the aggregate electrical activity from up to 6 cm$^2$ of the brain surface, and hence from many millions of neurons.

The time evolution of generalized LMC statistical wavelet entropy (EEG signal shown in Fig. 1) is shown in Fig. 4. As before, dashed and continuous lines, respectively, represent the obtained values when frequency bands $B_1$ and $B_2$ are

![Fig. 4. Generalized LMC wavelet statistical complexity, $C_W$, time evolution. The dashed and the continuous lines represent the wavelet entropy time evolution with and without, respectively, the contribution of the frequency bands $B_1$ and $B_2$ (muscular activity). The vertical lines represent the start and end of the epileptic seizure.](image-url)
included or not in the evaluation of $C_W$. The generalized wavelet complexity $C_W$ exhibits almost constant values, similar in the pre-ictal and ictal stages, when the analysis includes the bands $B_1$ and $B_2$, not including these two bands in the analysis yields quite different results. In the ictal stage the $C_W$-values are larger than in the pre-ictal one. Also, $C_W$ falls in the vicinity of 120 s corresponding to the tonic–clonic transition. This $C_W$-“dip” is associated to a marked NTWS-diminution, opposite to what occurs around either (i) 140 s (disappearance of the epileptic recruitment rhythm), or (ii) 158 s (seizure ending time), where the NTWS-values grow. It seems that a different dynamical regimes obtained at 120 s vis-a-vis the one at 140 s or 158 s. Again, similar results were obtained for the remaining TCES records.

In Fig. 5a we plot the time evolution of the EEG series in the $(H, C_W)$ phase space. The maximum and minimum possible amounts of complexity $C_W^{\text{max}}$ and $C_W^{\text{min}}$ are drawn as a function of $H$, for the number of wavelet resolution levels used in the quantifiers’ evaluation ($N = 4$) [36]. The values corresponding to the pre- and post-ictal stages are clearly concentrated in the zone of both relatively high entropy ($H > 0.8$) and intermediate complexity (at the “eastern” part of the diagram), while a very different behavior can be associated with the ictal stage (circles and triangles). Moreover, as can be observed in Fig. 5b, it is possible to clearly distinguish between tonic (circle) and clonic (triangles) stages. This tonic–clonic distinction is one interesting contribution of the present work. Fig. 5b depicts data corresponding to the interval 97.5–140 s, associated with the epileptic recruiting rhythm. We see that the complexity is higher in the tonic 97.5–120 s stage than in the clonic 120–140 s one. Moreover, EEG “trajectory” tends to remain close to $C_W^{\text{max}}$ during the tonic stage, while it tends to approach the minimum complexity path $C_W^{\text{min}}$ as the trajectory evolves towards the end of the recruiting rhythm (140 s). These results are of an instructive character, notwithstanding the fact that a clear frontier between the two phases is not always discernible.

In Figs. 6 and 7 the mean values and the corresponding standard errors of NTWS and generalized wavelet statistical complexity $C_W$ for pre-ictal and ictal stage for the 20 epileptic seizures are presented. In reference to the NTWS as a measure of the degree of order/disorder, we can say that the NTWS presented lower values in the ictal than in the pre-ictal phase. In particular, if all frequency bands are included in the evaluation (see Fig. 6a), the differences between these mean values ($\Delta H = \langle H^{\text{ictal}} \rangle - \langle H^{\text{pre-ictal}} \rangle < 0$, $p = 0.6737$, using a one-sample $T$-test) are negative in 50% of the cases, but the number of negative differences increases up to 95% ($\Delta H < 0$, $p < 0.0001$, using a one-sample $T$-test) if the high-frequency bands ($B_1$ and $B_2$), mainly associated with the electromyographic activity, are excluded (see Fig. 6b). In contrast, the generalized wavelet statistical complexity $C_W$ present higher values in the ictal than in the pre-ictal phase. In particular, if all frequency bands are included in the evaluation (see Fig. 7a), the differences between these mean values ($\Delta C_W = \langle C_W^{\text{ictal}} \rangle - \langle C_W^{\text{pre-ictal}} \rangle > 0$, $p = 0.9513$, using a one-sample $T$-test) are positive in 25% of the cases, but the number of positive differences increases up to 85% ($\Delta C > 0$, $p = 0.0002$, using a one-sample $T$-test) if the high-frequency bands are excluded (see Fig. 7b). Consequently, we can associate a more ordered behavior...
with higher values of generalized LMC complexity to the brain electrical activity during an epileptic seizure.

The electrophysiology of generalized tonic–clonic seizures has not yet been fully understood. There are many descriptions of the typical pattern of EEG activity which accompany these seizures but few detailed or quantitative analyses are given. One of the main reasons for this situation is that, immediately after this kind of
seizure begins, muscle activity starts leading to artifacts which obscure the EEG data
[12]. The description of the pertinent data suggests that generalized tonic–clonic
seizure EEG data exhibit a complex time-evolution. There are also reports on spatial
variation on their manifestation, despite their classification as “generalized seizures”
[12,29,39]. Yet, until quite recently, there are no studies attempting to investigate and
quantify this complex dynamics.

Fig. 6. NTWS temporal average values (mean ± SE) over all time windows corresponding to pre-ictal and
ictal stages, for the 20 tonic–clonic epileptic seizures analyzed. With (a) and without (b), respectively,
taking into account the contribution of frequency bands B1 and B2 in the evaluation of total wavelet
energy. For the pre-ictal stage, time intervals that present artifacts have been excluded. In the horizontal
axes, the letters represent the patient and the number of the seizure occurrence.
Little information exists to explain the neurophysiology underlying generalized tonic–clonic seizures. A naive assumption is to believe that there are no variations in the degree to which cortical neurons participate in the generalized tonic–clonic seizures; however, the data that do exist do not support this view [12]. These data, instead, suggest that there are variations in the degree to which cortical neurons participate in the generalized toni–clonic seizures in both animal models and in

Fig. 7. Generalized LMC wavelet complexity $C_W$ temporal average values (mean ± SE) over all time windows corresponding to pre-ictal and ictal stages, for the 20 tonic–clonic epileptic seizures analyzed. With (a) and without (b), respectively, taking into account the contribution of frequency bands $B_1$ and $B_2$ in the evaluation of total wavelet energy. For the pre-ictal stage, time intervals that present artifacts have been excluded. In the horizontal axes, the letters represent the patient and the number of the seizure occurrence.
humans [12,40]. Some researchers have suggested that the “epileptic recruiting rhythm”, which manifests itself in the EEG after seizure-onset, is a cardinal feature of these epileptic seizures [29,12].

One critical point is the possible distortion due to spatial propagation of the seizure, since only data from the C4 electrode were analyzed and the sources of the seizures were mostly located in temporal locations (see Table 1). In order to overcome this problem, quantifiers based on ODWT were also applied to T3 and T4 electrodes, obtaining results similar to the ones reported with just the C4 electrode. Even though these additional electrodes present more artifacts, as compared with C4, the “recruitment epileptic rhythm” as well as a decrease of NTWS with increase of $C_W$ values for the ictal stage in comparison with the pre-ictal one were observed. For a quantitative analysis of the observed behavior in these two electrodes (T3 and T4) the above-introduced quantifiers based on ODWT were also evaluated. Some variation in the numerical values for the different quantifiers was observed. It is reasonable to assume that the different positions could provide additional information. Having EEG records at different places, a multichannel analysis should give more reliable results. The problem with the present set of data is inhomogeneity in the seizure localization, which invalidates multichannel analysis using an ANOVA test. New data are being collected in order to solve this problem.

5. Conclusions

The point of departure for the present considerations are the results of a recent evaluation of the chaoticity-quantifier\(^1\) as a function of time. There it was found that a chaotic behavior can be associated to the whole of an EEG signal [9,41]. We show here that the epileptic recruitment rhythm also exhibits larger values of generalized LMC complexity, in addition to being compatible with a dynamical process of spatial synchronization. As pointed out by many authors (see, for instance Refs. [26,27]), the coexistence of chaos with complexity is a manifestation of self-organization. We have thus suggested, on the basis of

(1) experimental EEG data and
(2) the use of appropriate statistical tools,

that one can make the following conjecture in the case of secondary generalized tonic–clonic epileptic seizures: the epileptic focus triggers a self-organized brain state characterized by both order and maximal complexity.

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\(^{1}\)“Chaoticity” refers to an evaluation of the biggest Lyapunov exponent without taking into account the stationary constraint.
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References