CHARACTERIZATION OF EPILEPTIC SEIZURE
DYNAMICS USING GABOR ATOM DENSITY

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Keywords: EEG, Epilepsy, Seizure, Signal analysis, Gabor Atom Density.
Abstract

Objectives: The study of epileptic EEG dynamics can potentially provide insights into seizure onset, evolution and termination. We propose a new synthetic measure based on time-frequency decomposition to provide detailed characterization of these dynamic changes.

Methods: The matching pursuit (MP) method allows for continuous time-frequency decomposition. We have developed a derivative of the MP method, the Gabor atom density method (GAD) that facilitates interpretation during the dynamic ictal period. The GAD analysis was applied to intracranial recordings of complex partial seizures (n = 43) of mesial temporal origin in 7 patients.

Results: Complex partial seizure occurrence is systematically associated with a GAD increase of 400±150%. The GAD increase coincides with the electrographical evidence of seizure onset. The similarity between seizures in a given patient is very high with uniform onset slope, maximum level and termination pattern. Global GAD responses over all channels can reveal detailed seizure propagation patterns including secondary independent foci and secondary generalization.

Conclusions: The GAD measure based on the MP decomposition is a reliable tool to detect seizure occurrence in long-term recordings, to differentiate seizures from artifacts on a multi-channel basis and to examine patterns of seizure propagation. The reproducible GAD pattern suggests consistent changes in signal inner structure and may provide new clues about seizure dynamics and evolution.

Significance: The GAD method can provide information about seizure dynamics that can contribute to methods of seizure detection. These analyses may lead to better understanding of seizure termination and help facilitate application of responsive seizure control devices in humans.
1. Introduction

Epileptic seizures are abnormal, temporary manifestations of dramatically increased neuronal synchrony, either occurring focally (partial seizures) or bilaterally (generalized seizures). The hallmark of partial seizures (simple or complex) is the evolution of seizure activity initially beginning at the seizure focus and then followed by variable spread to adjacent or remote cerebral regions, at times resulting in secondarily generalized seizures. The recorded signals of this seizure activity are characteristically rapidly changing. The occurrence and dynamics of these seizures often appear to be unpredictable, although detailed time-frequency analyses reveal that multiple seizures in a given patient may have similar dynamics (Franaszczuk et al., 1998; Jouny et al., 2001). The cellular and network mechanisms that may contribute to or cause this increased synchrony are still the subject of active investigations.

EEG characteristics of epileptic seizures have already been correlated with various observations. Based on simple frequency analysis, Spencer observed a higher dominant frequency at onset for medial temporal onset seizures than for extra-temporal ones (Spencer et al., 1992a). Visual classification of complex partial seizure onset type has been proposed by Ebersole and Pacia (Ebersole & Pacia, 1996) using scalp EEG. Several studies have focused on correlating the EEG characteristics with the seizure type: ictal spike activity with cell loss in hippocampus (Spencer et al., 1992b), rhythmic or spike activity at onset with hippocampal gliosis (Park et al., 1996), lower frequency of rhythmic activity with neocortical temporal epilepsy (Ebersole & Pacia, 1996; Foldvary et al., 1997). All these studies use either visual identification of EEG patterns or simple Fourier transform to extract a dominant frequency.
consistency and reliability of GADs to precisely characterize epileptic seizures and give a more detailed image of the dynamics of these seizures.

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References


Characterization of epileptic seizure dynamics using Gabor atom density

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Understanding the changes in signal dynamics during a seizure can provide insights into potential mechanisms for seizure control. Interest in controlling these seizures has increased during the last decade, based on limited results of successful attempts to terminate evoked seizure activity by electrical stimulation (Lesser et al., 1999; Karcsik et al., 2000; Counce and Kuzniecky, 2001). Other interesting results are from in vitro experiments where adaptive fields were used to control epileptic seizure-like events in hippocampal brain slices (Gluckman et al., 2001). Recent results based on neural network models also indicate the possibility of interrupting bursting activity in connected neural sub-networks by using the appropriate stimulation at specific times (Kudela et al., 2001). To better study and apply these methods, it becomes more important to have a better understanding of seizure dynamics. This means not only being able to detect a seizure, but also to monitor and classify its evolution and its different phases. Unfortunately, ictal evolution is typically a dynamic and non-stationary process with signals composed of multiple frequencies. This can limit or complicate visual and other methods of analysis.

There is growing interest in examining EEG changes using new time–frequency analysis and various non-linear dynamic approaches (see selected review in Le Van Quyen et al., 2001). While many investigators are focusing on the possibilities of seizure prediction offered by non-linear techniques, new time–frequency methods appear more promising to describe intrinsic properties of the signal. It has been suggested that the MP method is one of the best candidates for a universal method of parameterization of EEG (Durka and Blinowska, 2001). The decomposition produced by the MP method provides information about both rhythmic and transient brain activity and also provides detailed continuous quantitative analysis of the signal recorded from seizures. The advantages of the MP method include, the ability to provide time–frequency decompositions of even the most rapidly changing signal, and the fact that the method can be appropriately applied to linear, non-linear or unclassified signals.

Based on time–frequency decomposition, the MP algorithm can be used to describe the contents of a signal using single elements called atoms. Each atom can be characterized by its position in time and frequency and by its amplitude, scale and phase. The wide variety of information available by this method presents numerous possible areas of investigation. In the initial applications of the MP method to intracranial recordings of mesial temporal seizures, MP decomposition used a time–frequency plot to monitor the rapidly changing signals (Franaszczuk et al., 1998). The period of organized rhythmic activity (ORA) that occurred after seizure initiation was found to have a predominant peak frequency of 6.5–8.3 Hz in seizures recorded from 8 of 9 patients. This ORA was a signal of lower complexity than that during seizure onset or termination, and had a monotonic decline in predominant frequency during seizure evolution. Another study compared the signal complexity assessed by the MP analysis to a standard equation of known complexity (Bergey and Franaszczuk, 2001) to link the number of atoms to the usual definition of complexity. This study suggested that changes in signal complexity preceded seizure termination of mesial temporal onset seizures. Other previous applications of the MP method include analyses of evoked potentials, routine EEG and sleep (Blinowska and Durka, 1994; Allen et al., 1995; Shen et al., 1996). Despite the large amount of information provided by MP, a compact representation is desirable as a first basis to monitor composite changes. This does not preclude concomitant use of other information in the analysis of the signal.

In the studies reported here, we describe for the first time a measure derived from the MP analysis, which we have designated the Gabor atom density (GAD), as a primary tool to monitor changes in signal characteristics. Principally based on the number of atoms obtained during the decomposition, we demonstrate that the GAD measure is a reliable tool to assess the inner structure and dynamics of the seizure signal. We describe adaptations of the MP technique to fit the specific needs of seizure analysis and ways to improve results by adding criterion to the analysis. We report various physiological conditions that test GAD reliability in a more general context.

2. Methods

2.1. Matching pursuit algorithm

The matching pursuit (MP) algorithm is an improvement in time–frequency analysis combining the advantage of short-windowed Fourier transform and wavelet analysis. Basic windowed Fourier transform describes the signal in terms of atoms localized in time and frequency. Wavelet analysis offers decomposition in time and scale but frequency is computed from the scale. We chose MP because it can offer a more rich decomposition using time, frequency and scale parameters. To do so, MP uses a non-orthogonal dictionary of functions, without constraints on the scale and frequency parameters. As our purpose is to explore the structure of EEG signals during epileptic seizures, this use of a largely redundant dictionary gives us extended flexibility and the ability to provide a more detailed decomposition of the signal patterns.

We use the original Mallat and Zhang MP software (which can be found at ftp://cs.nyu.edu/pub/wave/software). The detailed description of the method can be found in Mallat and Zhang (1993). We will only present here the general principle of the MP method using the complex notation. The software provides decomposition in discrete real atoms. A more detailed description of the stopping criteria of the algorithm will be presented in the next subsection.
The MP algorithm is designed to compute a linear expansion of a signal \( f \) over a set of elementary functions — called atoms — in order to best match its inner structures. This is done by successive approximations of \( f \) with orthogonal projections on elements of the dictionary of functions \( g \). The dictionary is composed of translated and modulated discrete Gaussians (Gabor functions), discrete Dirac functions and discrete complex exponentials. Gabor functions are the functions which best represent signal in the time—frequency domain because they possess the smallest product of effective duration by effective frequency. After \( m \) iterations, the MP decomposes a signal \( f \) into:

\[
f = \sum_{n=0}^{m-1} C_n g_n + R^m f
\]

with \( C_n = \langle R^g, g_n \rangle, m > 0 \) and \( R^0 f = f \).

The coefficient \( C_n \) is the inner product of the residue \( R^f \) with the atom \( g_n \). \( R^m f \) is the residual vector after \( m \) iterations. Gabor time—frequency atoms used are defined, for any scale \( s > 0 \), frequency modulation \( \xi \), and translation \( u \), by:

\[
g_s(t) = \frac{1}{\sqrt{I}G} \left( \frac{1 - u}{s} \right) e^{i \xi t} \tag{2}
\]

with \( g(t) = e^{i \xi t} e^{-\alpha t^2} \) and \( \gamma = (s, u, \xi) \), where \( 1/\sqrt{I}G \) normalizes the norm of \( g_s \) to one.

Based on the properties of the decompositions and on the fact that the dictionary is complete (Mallat and Zhang, 1993), we can write an energy conservation equation for the signal \( f \):

\[
\|f\|^2 = \sum_{n=0}^{m-1} \|R^g, g_n\|^2 + \|R^n f\|^2
\]

with \( \lim_{m \to \infty} \|R^n f\|^2 = 0 \).

As \( \|f\|^2 \) is the total energy of the signal, we will further refer to \( \|R^g, g_n\|^2 = |C_n|^2 \) as the energy of the atom, and \( \|R^n f\|^2 \) as the energy of the residue. If we define:

\[
E_f(t, \omega) = \sum_{n=0}^{\infty} \|R^g, g_n\|^2 Wg_n(t, \omega) \tag{4}
\]

we have also:

\[
\|f\|^2 = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} E_f(t, \omega) dt d\omega
\]

In this case \( E_f(t, \omega) \) can be interpreted as an energy density of \( f \) in the time—frequency plane where \( Wg_n(t, \omega) \) is the Wigner distribution of Gabor atom \( g_n(t) \):

\[
Wg_n(t, \omega) = Wg\left( t - \frac{u_n}{s_n}, \omega - \xi_n \right) \tag{6}
\]

for \( \gamma_n = (s_n, u_n, \xi_n) \)

with \( Wg(t, \omega) = 2 \exp\left( -2\pi(t^2 + (\frac{\omega - \xi}{2\pi})^2) \right) \tag{7} \)

The time—frequency energy distribution \( E_f(t, \omega) \) is used for visualization of the structure of the decomposed signal and is represented by the sum of 2D-Gaussians (Eq. (4)) whose locations and variances along the time and frequency axes depend upon the parameters \( (s, u, \xi) \) and whose amplitudes are proportional to the energy of the atom \( |\langle R^g, g_n \rangle|^2 \).

2.2. Decomposition criteria

The decomposition in itself does not set the number of iterations to perform, but sorts atoms by largest inner product with residual — i.e. by energy. Different criteria can then be implemented to stop the process. The first criterion, introduced by Mallat (Mallat and Zhang, 1993), is based on the idea of limiting the decomposition to coherent structures. We will further reference it as the ‘coherence criterion’ but we point out that this is not related to the signal coherence terminology frequently used in signal processing. This criterion is based on the decay of energy of the residue:

\[
\lambda(R^n f) = \sqrt{1 - \frac{\|R^{n+1} f\|^2}{\|R^n f\|^2}} \tag{8}
\]

Mallat defined the coherent structures of the signal as the first \( m \) atoms \((g_n)_{n=0, \ldots, m}\) that have a higher than average correlation with the residue \( R^n f \). If \( W \) is discrete Gaussian white noise, this criterion can be written as:

\[
\lambda(R^n f) > E(\lambda(R^n W)) \tag{9}
\]

Based on numerical approximations, the expected value \( E(\lambda(R^n W)) \) can be derived from the number of points \( N \) of the signal used during the analysis:

\[
E(\lambda(R^n W)) = (2.07647 - 0.089091 \log(N)) \sqrt{\log(N)} N \tag{10}
\]

This expected value is then used as threshold for the rate of decay of energy of the residue (Eq. (8)).

One can stop the decomposition by combining several criteria. For example, one can add to the coherence criterion, a second one based on the percentage of energy of the original signal, already explained. Despite the frequent use of the percentage of energy, this criterion can be misleading, as the results cannot be explained without the total energy plot. We rather chose to add a criterion based on the energy of the last atom added, equal to \( |C_n|^2 \), that can be seen as the energy resolution achieved, as the decomposition sorts the atoms by decreasing energy. The advantage of using such a threshold is that the decomposition will continue up to this same energy resolution, regardless of the occurrence of any energy surge in the signal or of an atom with a large modulus \( |C_n|^2 \) in the decomposition. The

\[
\lambda(R^n f) > E(\lambda(R^n W)) \tag{9}
\]
Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Focus area</th>
<th>Number of CPS</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>38</td>
<td>Left mesial temporal</td>
<td>10</td>
<td>F</td>
</tr>
<tr>
<td>P2</td>
<td>47</td>
<td>Left mesial temporal</td>
<td>1</td>
<td>M</td>
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<td>Left mesial temporal</td>
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</tr>
<tr>
<td>P7</td>
<td>11</td>
<td>Right mesial temporal</td>
<td>5</td>
<td>M</td>
</tr>
</tbody>
</table>

Criterion can be written simply as:

$$|c_n|^2 \leq \text{Threshold}$$  \hspace{1cm} (11)

We will refer to this method as the 'energy resolution criterion' or the 'energy threshold criterion'. As the energy of each atom $|c_n|^2$ is the square value of the modulus of $c_n$, we can also use an equivalent threshold on the modulus $|c_n|$.

We define the GAD as the number of atoms $m$ obtained during the decomposition divided by the size of the reconstructed time–frequency space. For each window, the range of time and frequency are, respectively, $R_t = N/\ell(F_s)$; $R_f = F_s/2$, where $N$ is the number of points in the window and $F_s$ the sampling frequency. The density of atoms over that space is:

$$d = \frac{m}{R_t R_f} = \frac{2m}{N}$$  \hspace{1cm} (12)

Applied to a finite-length window, this density can be used to characterize the richness of the signal during this period. We will use the term 'GAD analysis' to refer to the decomposition performed using the MP algorithm developed by Mallat and Zhang (1993), with the additional energy resolution criterion introduced here. The number of atoms $m$ is dependent on the signal but is much smaller than $N$ in most cases, so typical values of GAD range from 0 to 2.

2.3. Clinical data

We analyzed continuous EEG data recorded from intracranial electrodes in patients with intractable complex partial seizures (CPS). These patients were being monitored prior to seizure surgery. Intracranial EEG recordings were used in instances where seizure localization from scalp electrodes was insufficient for localization of seizure foci or if functional mapping of eloquent cortex was important. Recordings typically included a 32–48 contact subdural grid over the lateral temporal neocortex and additional subdural strips recording from mesial and basal temporal regions. Additional frontal strips were often also used. The patients selected for these analyses were those that were determined to have mesial temporal lobe seizure onset. Patient 3 had a low grade tumor involving the mesial temporal structures, the other 6 patients had non-lesional epilepsy (including mesial temporal sclerosis).

The intracranial EEG recordings from all seizures ($n = 43$) were reviewed and classified. Patients included 4 men and 3 women, from 11 to 56 years old (cf. Table 1). We included only CPS; auras and simple partial seizures were not included in the analyses; similarly subclinical events were not analyzed. All seizures analyzed were complex partial, however, some secondarily generalized. Seizures terminating suddenly in all intracranial channels were included with those seizures that had asynchronous termination or evidence of secondary foci.

2.4. Analysis

Raw EEG data were low-pass filtered (70 Hz), digitized at a sampling rate of 200 Hz using a Telefactor™ system. Pre-processing included a second digital low-pass filtering (Type FIR, order = 50, $F_c = 50$ Hz) and down-sampling at 100 Hz. Decompositions are performed on single channel signals and repeated for all valid channels. We excluded from analysis channels that were flat, not connected or continuously contaminated by artifact. GAD analysis was applied using a 1024-point window ($10.24$ s) with 200-point shift (2 s) between each consecutive window to achieve a final temporal resolution of 2 s. To compute each density value, we use the 1024 previous points, to allow the procedure to potentially be used for online detection. As the GAD is normalized by the window length, the window length parameter does not affect the density results, but only the frequency resolution on the time–frequency reconstruction. Decomposition is stopped using coherence criterion. Atoms found during the decomposition were reprocessed to apply the energy resolution criterion.

In order to achieve the most effective analysis of the seizures, we have added to the original MP algorithm a new criterion based on the energy resolution. We adjust this energy resolution threshold to enhance density differences between selected periods (seizures) and the background level. From the first seizure of each patient, the difference is calculated between the GAD maximum level during the ictal period and the mean GAD level over 100 points (200 s) before seizure onset. This difference is computed for energy thresholds ranging from 0 (no threshold) up to $10^6$ $\mu$V$^2$ – equivalent to value of the square root of the energy ranging from 0 to 1000 $\mu$V. Subsequently, we use the term GAD$_c$ for the GAD obtained with the original coherence criterion and GAD$\tau$ for the GAD obtained with the energy threshold criterion.

We have compared seizure characteristics such as onset time and duration based on clinical evaluations with results obtained from the GAD$\tau$ method. Clinical detection of seizures was performed by neurologists caring for the patient in the monitoring unit. These observations were reviewed and confirmed by review of the videotaped records of the seizures. Determination of seizure focus, onset and
termination time for seizures was based on electrophysiological criteria from the intracranial recording data. Onset and termination time were measured from one electrode close to the focus of initial seizure onset regardless of the occurrence of subsequent secondary foci. Seizure characteristics based on GAD$_T$ values are determined using both computational and visual procedures. We performed the onset and termination determination in two steps. As seizures seemed to be associated with increases in GAD$_T$ levels, a threshold detection method was applied to detect significant increases in GAD$_T$ levels. The onset ($t = 0$) was set as the last inflexion point before GAD$_T$ levels increase over the threshold. The threshold itself was fixed as the mean value over a reference period plus 3 times the standard deviation. On the same basis, termination was defined as the first inflexion point after the GAD$_T$ level returned below this threshold. A second step, a visual examination, was performed to adjust the inflexion points to visual evidence of seizure onset, when the automatic detection was not precise enough. Using this adjustment, the onset point was never changed by more than 3 samples (6 s) from the original detection. At times seizure termination was abrupt in all channels, at other times the seizure termination was less absolutely defined and therefore the seizure endpoint was more challenging to define (see for example, bottom panel in Fig. 6). Nevertheless, some rules were used to do so. Termination definition required: a significant drop in the GAD$_T$ level compared to the maximum during the seizure, a level around the inter-ictal level or below, no significant increase immediately after (except artifact or other identified events such as abrupt state transitions such as awakenings). For comparison of levels, we define the GAD$_T$ level for the seizure as the highest value during the seizure. The reference level is an average value computed over a 5 min inter-ictal period starting at the beginning of each recording for each seizure. These inter-ictal periods were at least 15 min prior to the onset of the seizure. For the slope, we consider a constant window of 5 points (8 s) including the onset point. The window length has been set to a fixed value to be consistent through all the seizures but short enough to be compatible with even the shortest rise time.

To compare GAD$_T$ parameterization of seizures with the time of onset and duration to the clinical evaluation for all patients, we performed one-way analysis of variance with repetition equal to the number of seizures for each patient. The significance of the difference between times of onset between both groups were then assessed by simple $t$ test and significance of the difference of duration by a paired $t$ test. Significance threshold is set at $P = 0.05$. Similar analysis of variance has been done on parameters used to characterize the GAD time course pattern during a seizure.

Computations were done on a cluster of 15 computers. Each node is equipped with a AMD Athlon™ 1 GHz processor and running Linux RedHat™ 7.1. Data were distributed and processed simultaneously on all nodes. Processing time is dependent on the signal content. Average speed is 12 s of processing per minute of signal per channel: 24 h of data from 48 channels was computed in 15 h on our cluster. Even though the computation cost of MP analysis is significantly higher compared to basic fast Fourier transform (FFT), the power of modern computers allows online analysis of several channels (~5) with even a low range PC.

3. Results

To understand the effect of the new threshold criterion, we have computed for a seizure (using the original coherence criterion) the distribution of the modulus of the atom coefficients $C_n$ obtained for 3 different periods: the pre-ictal period, the ictal period, and the post-ictal period. We have selected the same window length, 1 min, for the 3 periods based on the length of the seizure. In Fig. 1, we have represented, for one seizure of patient P2, the distribution of $|C_n|$ for each period. In this example, the distribution during the ictal period of the seizure is clearly shifted toward higher energy compared to the inter-ictal distribution. This shift is related to the increase in EEG signal amplitude, but there is also a change of shape toward a log-normal distribution with an additional peak of high energy atoms. In contrast, the distribution for the post-ictal period is more similar to the inter-ictal one but with a slight but clear shift toward lower energy levels. This is consistent with the visual observations of the signal in the post-ictal period where there is often marked depression of the signal. Applying the energy resolution criterion consists of counting, for each distribution, the atoms above a fixed threshold in energy. We indicate by the vertical dotted line the optimum threshold of energy for this seizure. For an energy threshold of approximately $4 \times 10^4 \mu V^2$ – equivalent to a modulus of
energy of the signal cannot be decomposed into atoms with \(|C_n|^2\) above the threshold used.

In contrast to these variations, the GAD_C does not present any clear changes during the ictal period except a slight increase in variability. Meanwhile, GAD_T presents a clear increase starting at the seizure onset and lasting approximately 1 min. We can observe that with the threshold we have chosen, GAD_T and GAD_C have almost equal values during the ictal period and similarly for Pct_T and Pct_C values. That means that the modulus of the coefficient \(C_n\) for the smallest coherent atom during the ictal period is almost equal to our threshold. These results confirm that this threshold value optimizes the difference between the inter-ictal and ictal periods but also reveal that a change in distribution of atoms can be monitored by a measure as simple as the percentage of energy explained.

Any further reference to GAD_T indicates the use of the common threshold value selected previously for the energy resolution criterion. This threshold cannot be directly interpreted as an amplitude value of the EEG trace. Indeed, the maximum amplitude of the energy density reconstructed for one atom is the product of the modulus of the coefficient \(C_n\) by the Gabor function itself. The maximum value of the Gabor function is variable; only the energy of the Gabor function is normalized to one. Therefore, even if the

200 \(\mu\)V, we obtain the highest difference in the number of atoms between the ictal period and the inter-ictal one. Subsequently, in order to compare GAD measures obtained for all the seizures, we want to use the same energy resolution, and to do so we have selected a common threshold to apply to all seizures and to all channels.

We determine this common energy threshold by testing the method with the first seizure of each patient (Fig. 2). When applied to these seizures, the coherence criterion, equivalent to an energy threshold value of 0, provides the best results in only two cases. The best energy threshold for the 5 other patients is in the range from \(6.4 \times 10^3\) to \(48 \times 10^3 \mu\)V\(^2\) (square root between 80 and 220 \(\mu\)V).

Considering the pattern of decreases with a higher threshold, an optimum value is selected for all the subjects at \(4 \times 10^4 \mu\)V\(^2\) (square root equal to 200 \(\mu\)V). It allows a sufficient sensitivity without being in the lower part of the graph where results are more seizure-dependent. With this threshold, we can expect a more uniform density increase for the seizure with a density difference around 0.3.

To visualize the efficiency of the energy threshold method compared to the coherence method, we compute and compare the percentage of energy explained with both criteria, respectively, Pct_C and Pct_T, and the corresponding GAD, respectively, GAD_C and GAD_T, for one complex partial seizure of patient P7 (Cf. Fig. 3). During inter-ictal periods, Pct_C is relatively stable around 98%. For the same period, Pct_T is significantly lower, around 90% before the seizure, and drops to 75% just before the seizure. These drops of Pct_T before the onset of the seizure mean that prior to the seizure and for a short period of time, 25% of the

Fig. 2. Threshold selection method. Density difference versus energy threshold. Each trace represents the results obtained for a seizure from a different patient. The selected threshold optimizes the density difference for the whole group.

Fig. 3. Percentage of energy explained and GAD for both coherence criterion (thick line) and energy resolution criterion (thin line). Time 0 indicates seizure onset.
Fig. 4. Time–frequency energy representation of a GAD analysis of a complex partial seizure using coherence criterion (Patient P2). Upper panels: EEG traces for 4 different periods (inter-ictal, ictal 1 early in seizure, ictal 2 later in seizure, and post-ictal). Lower panel: color-coded time–frequency energy plot of the signal (from contact LBT 58) obtained by reconstruction of the atoms. (Red: high energy, Blue: low energy). Energy scale is logarithmic. Superimposed over this plot is the corresponding GAD\(_T\) (black trace).

Fig. 5. Color-coded GAD\(_T\) time course for all channels for 3 different patterns of seizure evolution recorded for patient P1. (Red: high GAD\(_T\); Blue: low GAD\(_T\)). Left code indicated different grid localization on the brain (LBT, Left basal temporal; LFG, Left frontal grid; LFT, Left fronto-temporal; LOG, Left occipital grid; LPG, Left parietal grid). Black arrows indicate focus.
threshold can be expressed in microvolts, the 200 μV value cannot be related to an amplitude threshold on the EEG trace.

To illustrate the decomposition produced by the GAD analysis, we have reconstructed the energy density over the time-frequency plane for one entire complex partial seizure (Fig. 4). The 4 traces at the top of the figure show 10 s windows of the corresponding EEGs from different epochs. The first epoch is from the pre-ictal period, there are then two ictal epochs shown, and one from the post-ictal period. Variations in the distribution and density of atoms on the time-frequency plane are reflected by GAD_T (Fig. 4).

An increase in GAD_T indicates that a larger number of atoms is needed to correctly represent the EEG signal up to the resolution selected. For example, during the ictal period, the time-frequency plot displays a higher number of atoms which indicates that the decomposition process needs more atoms to match the signal structure during this ictal period compared to the inter-ictal period. The time-frequency plot also shows that not only the number of atoms is different during the seizure, but their frequency and duration distribution also changes dramatically. During the inter-ictal period, atoms are concentrated mainly in the delta and theta frequency band to match delta and theta EEG activities. During the seizure initiation period, more low-frequency atoms are needed as are more atoms with short duration, which appear as fine vertical lines. These short duration atoms, most of the time, match the intracranial electroencephalographic (ICEEG) pattern of the spikes occurring in the initiation period of the seizure. During the ictal period, GAD_T analysis reveals a different spectral signature. The period of organized rhythmic activity is characterized by high-energy atoms. More complex inter-ictal periods often have much more heterogeneous patterns of atoms with no well-defined apparent structures. The post-ictal period exhibits a low GAD_T level associated with a distribution mainly in the low-frequency range (delta).

We will use two representation modes for GAD_T. Single channel GAD_T values will be shown as a trace; multiple seizures can be displayed at the same time. Multiple channel results will be shown using color-coded GAD_T values for all channels (Fig. 5).

To show the GAD_T time course for a large number of seizures, we displayed 16 seizures from 3 different patients (P4, P5 and P7; Fig. 6). We observed for each seizure in a selected patient that there was a typical pattern for the GAD_T. The ictal period of the seizure is associated with a significant increase in GAD_T relative to the pre-ictal and post-ictal levels. While patterns for complex partial seizures may appear different from one patient to another, the similarity between seizures for a given patient is high. The similarity of characteristics such as slope, duration and global shape of the GAD_T response reveals a well-reproducible phenomenon for the same patient. Between patients, the termination patterns reveal the most differences because of the differences in the patterns of termination, which can be abrupt, preceded by a peak or with a slow decay. Patients P4 and P7 also exhibit very similar levels before and during the ictal period. Patient P5, who had seizures during sleep, is in the same sleep stage each time the seizure occurs and exhibits higher background GAD_T levels.

Fig. 6. GAD_T Individual patterns during several mesial temporal onset complex partial seizures for three patients. Panel A: 9 seizures (Patient P4). Panel B: two seizures (Patient P5). Panel C: 5 seizures (Patient P7). Time 0 is the seizure onset determined with GAD_T. A 3-point moving average filter has been applied on each trace for the graphical display.
We compare the parameterization of the seizure by both GAD$_T$ and clinical methods. Analysis of variance for the difference between onset times reveals that the PATIENT factor was not significant ($F = 2.304; P = 0.055$). Using the whole group of seizures ($n = 43$), we tested the H0 hypothesis that the onset times were identical with both methods. With a paired $t$ test, we could not reject H0 ($t = -1.209; P = 0.233$), the clinical and GAD$_T$ onset time of seizures matched. We also compared the duration assessed by both methods. Again, the analysis of variance indicated that the PATIENT factor was not significant ($F = 1.836; P = 0.120$). We tested the hypothesis H0 that both durations are the same. The paired $t$ test between both duration rejected H0 ($t = 8.777; P < 10^{-5}$), the two measures gave significantly different results. The GAD$_T$-based duration is significantly greater than the clinically-based visual analysis duration by $17.7 \pm 13.2$ s. The GAD$_T$ estimation is based on 10.24 s window analysis and the result of this technical procedure is a smoothing effect which increases the duration by one window length. However, even after correction for the effect, the GAD$_T$-based duration is greater than the clinically based one by $7.5 \pm 13.2$ s.

To describe the GAD$_T$ time course over a seizure, we focused on 4 different features extracted from the GAD$_T$ trace: the slope at the onset, the maximum level during the seizure, the percentage of increase compared to the background level and the duration of the seizure (Table 2). We also included in the table the difference between background level and seizure level. Analysis of variance reveals that all these parameters are patient dependent. At the seizure onset, we measured slope around $15 \times 10^{-3}$ s$^{-1}$, but individual values range from $5.0 \times 10^{-3}$ to $24.8 \times 10^{-3}$ s$^{-1}$. In fact, if we consider patients for which the slope value is more than one standard deviation from the mean value, patient P6, who has mean slope values below $10 \times 10^{-3}$ s$^{-1}$ is the patient with one of the longest seizures, 2 min 36 s. At the other extreme, patient P4 with a slope of $24.8 \times 10^{-3}$ s$^{-1}$ has short seizures, with durations less than 1 min. The level comparison shows that ictal levels are around $0.4 \pm 0.1$ and are higher than the inter-ictal levels by $0.28 \pm 0.06$ on the density scale. This is equivalent to a $400 \pm 143\%$ increase; individual increases ranged from 246 to 611%. Our limited number of patients does not allow us to explore more nor to conclude about possible relations between these parameters.

To compare the GAD$_T$ time course during a seizure to the GAD$_T$ behavior during other physiological EEG events, we compared, for the same patient (P5), 90 min containing a 1 min seizure and a following 24 h seizure-free period after an interruption due to an unexpected clinical intervention. As shown in Fig. 7, the GAD$_T$ increases during the seizure — indicated by the arrow — and reaches approximately a value of 0.3 on the density scale. On the rest of the trace, we can observe the physiological variations of GAD$_T$ related to different periods of the day. The sleep onset is around 3:00 a.m. At night, during the indicated sleep period, the GAD$_T$ varies following the sleep cycle. In fact, GAD$_T$ increases during non-rapid-eye-movement (NREM) sleep stages compared to rapid-eye-movement sleep (REM) sleep and waking. The pattern during NREM sleep stages could be related to increases in delta activity associated with transition into deeper sleep stages. During the day, similar increases can be observed when the subject took a nap around 2:30 and 4 p.m. Nevertheless, all these variations stay in a range below the seizure level; GAD$_T$ levels during sleep never exceed 0.15—0.2.

We have compared the GAD$_T$ responses of 3 different seizures using a complete overview of all the available channels. In Fig. 5, the GAD$_T$ for each channel is represented as a horizontal line of the image. The GAD$_T$ values are color-coded from blue (low) to red (high). We have represented in this figure, 3 different seizures of patient Pl. All the seizures are CPS but their evolution was different. The left panel is the most typical CPS for this patient, beginning in the mesial
temporal regions (Left basal temporal (LBT) subdural strip) with regional involvement of temporal and, to a lesser degree, frontal regions. The GAD$_T$ responses over the entire grid array show the different regions involved (red segments). The, apparent, non-contiguous positions of the segments results from the display of channels, grouped by grid. The middle panel shows the GAD$_T$ responses for a CPS with a secondary focus. We noted that the same areas are involved at the onset of the seizure, but the frontal areas (left frontal grid (LFG) grid) are now more involved, last longer and result in secondary seizures, which persist longer than the original focus. The right panel is a CPS that secondarily generalizes. We can observe, as before, the primary involvement of areas LBT, LFG and the lower part of left fronto-temporal (LFT) but the seizure spreads very rapidly to a large number of areas and finally generalizes to the entire set of channels. In this case, the termination is abrupt and simultaneous in all channels. Interestingly this secondarily generalized seizure is of shorter duration that the partial seizure shown in the middle panel.

As shown in Fig. 7 the GAD$_T$ level during a seizure is above the normal EEG activity during day or night and even during an artifact period during this 24 h period. Nevertheless, large artifact can still produce GAD$_T$ response in the range of seizure levels. We show in Fig. 8 the difference between the response of the GAD$_T$ measure to an artifact and a CPS when we used the representation with all channels. In this figure (patient P1), an artifact is clearly visible at 240 s before the onset of the seizure (marked as time 0). It appeared as a solid vertical black line, synchronized over all the channels. For comparison, the CPS has a focal initiation, a subsequent variable propagation and a heterogeneous time frame. This allows for reliable differentiation between artifact and physiological changes.

**4. Discussion**

The main goal of this study is to assess the suitability of the GAD measure to analyze rapidly changing electroencephalographic manifestations of epileptic seizures. Despite the previous use of the MP algorithm to analyze similar kinds of data, this type of analysis remains infrequently used mainly due to the heavy computation requirements, and to the lack of extensive references. We attempt here to present an overview of the possibilities offered by a new modification of the MP algorithm dedicated to the processing of EEG signal and the results that can be expected from analyzing intracranial recordings of epileptic seizures with this algorithm.

The use of a supplementary criterion for stopping decomposition of the MP algorithm greatly enhances the efficiency of seizure localization when multiple channels are analyzed. Where normal coherence criterion can give variable results, energy threshold criterion gives reliable
and stable results using the GAD T amplitude obtained for a seizure. Instead of discarding amplitude variations of EEG signals by using normalized EEG or percentage of energy, we increased the efficiency of the algorithm by taking advantage of the changes in distribution of the modulus of the atom coefficients during the ictal period. While our results are still dependent on EEG amplitude, GAD T gives more information about the complexity of the signal structure than a simple energy measure. For example, a signal composed of a high amplitude sinusoidal component would have a high energy but a low GAD T, while a signal composed of several low amplitude components would have a low energy but a high GAD T. MP decomposition provides extensive information about time, frequency, scale, amplitude and phase of the different components of the signal. Time–frequency plot reconstruction is a convenient graphic way to represent the decomposition, but detailed analysis of characteristics of the atoms remains possible. GAD reduces the amount of information to a synthetic measure that allows changes to be easily monitored.

Using only the GAD T measure, the MP decomposition gives a reliable signature of CPS that can be easily recognized. It features a major increase in GAD T values compared to inter-ictal levels, with a very reproducible pattern for a given patient. It also exhibits similar patterns for all the seizures of all the patients analyzed, using the same parameter for the analysis. While average patterns cannot be represented due to the limited number of patients, the basic description of GAD T responses to epileptic seizures can be appreciated. The match of GAD T-based seizure onset and clinical onset based on electroencephalographic reviewing proves the consistency of the measure across patients and the usefulness of GAD T to detect seizure occurrence. Even though we observed a slight difference between clinical and GAD T-based measure of the duration, we still have the same reliability of this measure across patients. GAD T, based on single channel analysis, does not reveal any systematic changes preceding the seizure onset that could lead to a predictive technique. Nevertheless, it does not preclude the possibility of detecting such changes with combined GAD T analysis for multiple channels.

With the optimized threshold selected, one can characterize the seizure signature with several parameters. These parameters appear to be patient-dependent and can lead to a new way to quantify and describe the type of seizure for each patient. Due to the small number of patients in this study, we were not able, yet, to explore possible relationships between these parameters or between them and other clinical information. The contrast obtained in GAD T levels between seizures and inter-ictal levels of 400 ± 140% confirms the efficiency of adding new criterion to enhance this difference. The absolute value of this increase around 0.28 corresponds to the target value chosen during the selection of the threshold. This target value was defined using a 7 seizures set, out of 43; the measure appears to be very consistent and applicable to larger sets of data. The slope of the GAD T increases, at the onset, appears also to be interesting as its variations may be explained by a difference in the speed of the seizure process to fully recruit the regional area involved, and for the EEG activity to evolve to the full expression of the seizure activity. Such a parameter could be very interesting to explore in instances of, for example, generalized onset seizures. In the partial seizures, analyzed here, the slope of the GAD T was very consistent between seizures in a given patient suggesting a given dynamic pattern of the seizure onset.

To verify the specificity of the GAD T response to epileptic seizures, we applied the GAD algorithm to analyze 24 h seizure-free periods. The GAD T remained around 0.05 during quiet waking and ranged between 0.05 and 0.2 during sleep, nap period or active waking which including periods with artifact. Relation between GAD T and other physiological measures can be also very interesting considering this sensitivity to EEG changes during sleep. The increase in delta activity and in total energy during NREM sleep is a factor which greatly influences GAD T. However, the distribution of energy during these periods is modified and monitoring these changes with GAD T could give new insights into sleep related phenomena. In contrast to NREM, in sleep, which is easily monitored by the delta activity, there is not yet any EEG parameter to follow to understand the dynamics and homeostasis of REM sleep. Techniques to assess these high frequency components during REM, and especially the phasic period of REM are of particular interest as increases in energy for the high-frequency band have been observed during these periods compared to the tonic phase of REM sleep (Jouny et al., 2000) and could be a marker of specific REM activity.

We also tested artifacts to explore the specificity of this method. While GAD T levels during artifacts remained below the levels of a seizure in the great majority of instances, very noisy data or a major artifact can cause a surge on GAD T levels close to the one obtained during a seizure. Even in this case, by extending the analysis to additional channels, one can obtain valuable information about the contamination based on GAD T. The GAD T signature of noise is quite discernable from seizure signature on the whole set of channels. Artifacts on intracranial recordings are often generalized artifacts affecting the whole set of electrodes or at least a whole grid or strip at a time. In this case, the high similarity of GAD T traces over the channels can easily differentiate seizure from artifact. Recognition techniques using simple neural networks could be developed to transform this visual detection procedure into a single parameter to monitor.

The GAD T response over the entire set of channels could be a very interesting tool to monitor seizure propagation patterns. The propagation pattern between a CPS with either secondary foci and a CPS that secondarily generalizes can be easily appreciated by comparing the GAD T for the whole set of channels. While we have limited our study to CPS originating from mesial temporal regions in this first approach, the GAD T...
time courses obtained raise the possibility of a more precise way to differentiate sub-types of seizures even within the CPS category. Different intra-seizure GAD_{T} patterns and seizure termination patterns exhibited by different patients can lead to additional classifications of these seizures that incorporate degree of spread and termination patterns. Combinations of features, such as onset time, slope of GAD_{T} at onset and duration could be used to create parameters characterizing the pattern of seizure dynamics.

The relevance of the GAD analysis for clinical purposes remains to be determined, as correlation with clinical information was not fully explored in this introductory study. Nevertheless, first observations indicate the use of an appropriate threshold gives very similar GAD values among patients for inter-ictal periods, ictal periods and even sleep periods. As the 24 h analysis revealed, the observation of the GAD trace over longer periods of time allows a very rapid detection of seizures and sleep periods. There is also growing interest in developing responsive systems (i.e. triggered by detection of seizure onset) of brain stimulation to terminate seizures in human. Using the GAD method to provide a detailed analysis of seizure dynamics may provide important insights into patterns of seizure activity that underlie seizure onset, as well as spontaneous and triggered seizure termination.

The MP algorithm was chosen as a tool to describe EEG signal structures because it gives very robust time–frequency decompositions. The use of a redundant dictionary is a necessary cost of this robustness. Other time–frequency decompositions, such as wavelet analysis, do not have the flexibility required for an exploration study of dynamic signals of unknown composition. Nevertheless, once seizure dynamics are better understood future applications, such as recognition of EEG patterns, could later be done using faster methods specially tuned using results from MP analysis.

Based on the MP algorithm, we have derived a new measure that we have designated the GAD. This measure, and the decomposition from which this measure is extracted, provide a new tool to identify epileptic seizure signatures. It also opens a broad spectrum of possibilities to investigate the properties of the EEG signal during these seizures based on the different characteristics obtained from the time–frequency decomposition. A natural extension of this preliminary work is to explore the frequency and scale distribution of these atoms during the different phases of the seizure. The GAD parameters including slope and level can also be investigated in relation to the sub-type of seizure. For this purpose, the new algorithm and its implementation will allow systematic computation of the GAD_{T} for multiple seizures of multiple patients and help to build a database of GAD_{T} time courses classified by seizure type and localization. Further applications can then test on a larger scale the consistency and reliability of GAD_{T} to precisely characterize epileptic seizures and give a more detailed image of the dynamics of these seizures.

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References


