Published in final edited form as:

Clin Neurophysiol. 2012 April ; 123(4): 658–669. doi:10.1016/j.clinph.2011.08.003.

Characterization of Early Partial Seizure Onset: Frequency, Complexity and Entropy

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Abstract

Objective—A clear classification of partial seizures onset features is not yet established. Complexity and entropy have been very widely used to describe dynamical systems, but a systematic evaluation of these measures to characterize partial seizures has never been performed.

Methods—Eighteen different measures including power in frequency bands up to 300Hz, Gabor atom density (GAD), Higuchi fractal dimension (HFD), Lempel-Ziv complexity, Shannon entropy, sample entropy, and permutation entropy, were selected to test sensitivity to partial seizure onset. Intracranial recordings from forty-five patients with mesial temporal, neocortical temporal and neocortical extratemporal seizure foci were included (331 partial seizures).

Results—GAD, Lempel-Ziv complexity, HFD, high frequency activity, and sample entropy were the most reliable measures to assess early seizure onset.

Conclusions—Increases in complexity and occurrence of high-frequency components appear to be commonly associated with early stages of partial seizure evolution from all regions. The type of measure (frequency-based, complexity or entropy) does not predict the efficiency of the method to detect seizure onset.

Significance—Differences between measures such as GAD and HFD highlight the multimodal nature of partial seizure onsets. Improved methods for early seizure detection may be achieved from a better understanding of these underlying dynamics.

Keywords

High-frequency; Complexity; Entropy; Early Ictal Onset; Partial Seizures; Seizure Detection

1 – Introduction

The detection, identification, and even prediction of epileptic seizures are paradigms that are hindered by the lack of understanding of the phenomena taking place at the onset of these events. Among the approaches taken to understand these dynamic changes is the analysis of electroencephalograms recorded continuously before, during and after epileptic events. But even today a clear classification of partial seizures onset features is not established; the

onsets of focal seizures are typically more subtle, more slowly evolving, and more heterogeneous than are the onsets of primary generalized seizures.

Over the past several decades, as the EEG has transitioned to digital recordings, classification of epileptic seizures based on electrographical features also evolved as previous visual characterization of features have been replaced by algorithmic evaluations of various descriptors of these seizures. Prior to the digital processing of the EEG recordings, visual characteristics of the EEG patterns were used as means of classification (Blume et al., 1984; Ebersole and Pacia, 1996). As spectral analysis became widely available, frequency parameters were added and are used today to assess the onset patterns in a more objective manner (Spencer et al., 1992; Srinivasan et al., 2005; Meier et al., 2008; Wetjen et al., 2009). A number of studies have paid particular attention to high-frequency components of the EEG and have focused on assessing if high-frequency oscillations (HFO) (Bragin et al., 1999; Staba et al., 2004) recorded ictally (Worrell et al., 2004) or interictally (Urrestarazu et al., 2007; Brázdil et al., 2010; Crepon et al., 2010) can be used to help identify the seizure onset zone. A growing number of studies have also investigated the potential changes in entropy and complexity in the EEG. While the concepts of complexity, entropy, and chaos have been rapidly expanding from their original domain of physics and mathematics (Baranger, 2002) into the domain of health sciences (Rickles et al., 2007) over the past decade, these concepts have sometimes been misinterpreted or confused and remain at the research stage for the time being (see conclusions in Stam et al., 2005). However the author also pointed out that anticipation and detection of epileptic seizures are the most likely fields of epileptology to be able to benefit from real world application of those concepts.

Applications of measures of complexity and entropy to epileptic seizures either in humans (Alarcon et al., 1995; Hu et al., 2006; Abasolo et al., 2007; Bruzzo et al., 2008; Tito et al., 2009) or in animals (Li et al., 2007; Ouyang et al., 2010) have been attempted but often included only limited datasets or limited set of measures. A systematic comparative analysis is still lacking. And while changes in complexity and entropy are typically associated with the dynamic evolution of a seizure, these are not characteristics that are appreciated from visual inspection of the ictal EEG.

We present here the first systematic application of multiple measures of complexity and entropy to intracranial ictal recordings of partial seizures to determine the early ictal changes of these measures. There are many definitions for both entropy and complexity and potential classifications of these methods were introduced by Wackerbauer (Wackerbauer et al., 1994) and Rapp (Rapp and Schmah, 1996). Attempts to compare the theoretical and applied advantages of those measures have grown over the last decade (Jimenez-Montano et al., 2002; Rosso et al., 2003; Ferenets et al., 2006; Adeli et al., 2007; Brooks, 2007; Hornero et al., 2008; Chen et al., 2009; Sabeti et al., 2009). The most common entropy measures are distribution-determined and provide a quantitative determination of the relative frequency of a specific event but are insensitive to the sequence of events. Complexity measures often address this deficiency by including a parametrization of the sequence of events. We focus our study on the relationships between the most commonly used spectral features and the measures of entropy and complexity for biological signals and their comparative efficiency when dealing with real world cases of seizure detection. Computation of several complexity measures rather than relying on a single measurement can provide a more comprehensive overview of the underlying processes (Bhattacharya, 2000; Watanabe et al., 2003; Brooks, 2007). All the measures investigated here are single channel analyses and focus on the pair of electrodes closest to the seizure focus. In an effort to better be able to identify changes that are relevant to the accurate detection of the onset of epileptic seizures, we investigate the characteristics of the very early period of seizure onset.

2 - Methods

Records from 45 consecutive patients (22 males and 23 females) with intractable partial epilepsy undergoing presurgical evaluations requiring intracranial recordings between 2004 and 2006 at the Johns Hopkins Epilepsy Center were selected for this study. Intracranial recording arrays included combinations of subdural multicontact grids and strips placed over the area of interest and targeted multi-contact depth electrode arrays. Typical implantation includes 64 to 128 electrodes in 4 or 8 contact strips and grid arrays with 16 to 64 contacts. Seizures were recorded using a Stellate™ system with Schwarzer amplifiers. A 300 Hz low-pass, Butterworth anti-aliasing filter (order=5 ; 20dB/oct) was applied prior to 16-bits digitization over a $\pm 3196 \mu\text{V}$ range. Analyses were carried out using bipolar montages using neighboring electrodes for improved localization of ictal onset activity. Events analyzed included sub-clinical seizures, simple and complex partial seizures with or without secondary generalization. All seizures were spontaneous events occurring over the course of the evaluation (5–7 days). Seizures arose either from awake or asleep state, however sleep staging is not possible on intracranial recordings without simultaneous scalp recordings so sleep stage at time of seizure occurrence is not available. Medications were reduced or discontinued in most patients during the evaluations to promote spontaneous seizure occurrence. Three hundred thirty one (331) seizures were available for analysis. Overall the time of occurrence of seizures were distributed evenly over the 24h period, with a circadian modulation of the number of occurrence with a maximum around noon. The average temporal distance between seizures per patient can be approximated with a log-normal distribution and values ranged from 10 minutes to 5 days, with a mean of 20 hours and a mode of 10.5 hours.

The research protocol was reviewed by the IRB and data were stored in compliance with HIPAA regulations. Seventeen patients were diagnosed with mesial temporal lobe epilepsy (MT), 5 with neocortical temporal lobe onset epilepsy (NeoT), 15 with extra-temporal lobe epilepsy (NeoXT) and 8 patients could not be classified due to multi-foci onset seizures or rapid bilateral spread; this group was labeled undetermined (UDT). The mean age value for the 45 patients is 27 ± 13 years.

The definition of electrographical onset (EO) is the earliest sign of epileptiform activity which subsequently evolves into seizure activity and is clearly distinct from the interictal activity. Visual identification of the onset is performed by scanning EEG traces backward from ictal periods back to the clear appearance of ictal components out of the interictal background activities. When the onset of activity was regional or involved rapid bilateral spread (UDT group) and could not be localized to a single electrode, one of the electrodes of the onset region was chosen for final analysis. EO was determined by a college of three reviewers, but no independent scoring was available to estimate inter-rater variability.

The analyses were all performed over a window length (W_L) of 4.096s and repeated four times with a shift of 1.024 seconds (W_S). The length of the window of analysis was chosen as a compromise between computational requirements, often requiring large amount of points, and statistical stationarity of the signal, which requires that the 1st and 2nd moment of the signal (mean and variance) do not vary over time. Some methods (eg. GAD) do not require signal stationarity. Others like the Higuchi fractal dimension who do can still be applied on shorter windows than typical fraction dimension estimators. Resulting data points are assigned to the time at the end of window W_L . We defined several periods: an interictal baseline period (I_{c0}) 60 seconds before the seizure onset, two preictal periods P1 and P2 prior to the onset of the seizure and two ictal periods S1 and S2 after the seizure onset (Figure 1). Each period P2, P1, S1, S2 includes 5 consecutive data points reflecting activity over 8.192s ($4 \times W_S + W_L$). As seen on Figure 1, data points right after EO were discarded to

avoid any overlapping influence between P1 and S1. Also, as these points were computed over windows overlapping before and after the EO during which the EEG can be highly non-stationary, estimation of some of the measures would have been less reliable. To maintain the S2 period within the duration of all seizures, S1 and S2 periods were selected to have a small overlap (P1 and P2 as well to mirror that time structure). Due to the weighting effect of moving windows, the overlap of the edge of the periods is not expected to have high impact of the correlation of those periods, however, interpretation of the comparisons P1-P2 and S1-S2 will be done with that caveat in mind. Parameters for all four periods were expressed as the standard deviation from the interictal baseline level Ic_0 to normalized measurements across all patients.

The measures used to characterize ICEEG properties are summarized below with extended technical details provided in Appendix A. Spectral measures include the total signal power (P). Although total signal power is not specific to any activity, the common increase in EEG signal amplitude during seizure activity makes it a default indicator of ictal occurrence. The frequency edge (F_e) – or spectral edge frequency – is a measure more commonly used in anesthesiology as a measure of sedation. The frequency edge is a simple indicator of the shifting of frequency in the EEG spectrum towards the lower frequency as sedation increases (Mahon et al., 2008). The power in specific frequency bands up to 300Hz were included, with band limits set to the conventional sleep and wake bands, δ : [0–4Hz[, θ : [4–8Hz[, α : [8–12Hz[while the higher frequencies were divided into β : [12–30Hz[, γ : [30–58Hz[and two high-frequency bands HF_{125} [62–125Hz[and HF_{300} [125–300Hz[. Open right bracket on the upper limit indicates the upper frequency is not included. Those high-frequency bands divisions were of our own choosing as there is no clearly established standard for high-frequency bands. Due to the bandwidth limitations of the recordings (low-pass 300Hz), activity in the fast-ripple range (200–500Hz) are not expected to be recorded, however ripples (80–200Hz) would be included in the two highest frequency bands we used.

Among the complexity measures used, the Gabor atom density GAD (Jouny et al., 2003) is a measure of complexity of the signal based on the matching pursuit (MP) time-frequency decomposition (Mallat and Zhang, 1993). GAD reflects the density of the EEG signal in regard to how many Gabor functions are extracted by MP to represent the signal. Applications of GAD to seizure onset detection have been proposed (Sorensen et al., 2010). The entropic non-triviality measure C_{JS} (Lamberti et al., 2004) was derived from previous work by Lopez-Ruiz (Lopez-Ruiz et al., 1995) and Anteneodo (Anteneodo et al., 1997). The measure is the product of a measure of entropy and a measure of disequilibrium which would be zero for totally random systems and totally predictable ones, but positive in between. C_{JS} allows one to distinguish between different degrees of periodicity, and was designed to ascertain the degree of unpredictability and randomness in a system. Plastino reported increases in complexity associated with a single seizure (Plastino et al., 2005). The Higuchi fractal dimension HFD (Higuchi, 1988) was introduced as an effective mean to assess the fractal dimension of a signal when only short windows of data are available. It can be used to measure the complexity and self-similarity of the EEG signal (Accardo et al., 1997). Paramanathan reported higher fractal dimension during ictal events in one single human patient (Paramanathan et al., 2008) while Päävinen reported decreased fractal dimension during seizures in rats (Päävinen et al., 2005). The Hjorth complexity (Hjorth, 1973) is a property of a signal, which in combination with activity and mobility was introduced by Hjorth in 1970, and redefined in 1973, to characterize the curve characteristics of the EEG traces. Specifically Hjorth complexity is a measure of the root-mean square frequency spread. It was used to identify patterns of seizure onsets (Alarcon et al. 1995) and for seizure detection (Päävinen et al., 2005). The Lempel-Ziv complexity LZC (Lempel and Ziv, 1976) is one of the most commonly used estimators of algorithmic complexity. After converting the signal into a binary strings by thresholding, the complexity of the binary

sequence is estimated based on the identification of repeated sequences and the achievable compression of the string based on the coding of those identified sequences. LZC has been tested to assess EEG changes during anesthesia (Zhang et al., 2001), in Alzheimer patients (Abasolo et al., 2006), and during seizures (Hu et al., 2006; Abasolo et al., 2007).

The entropy measures include the Shannon entropy ShEn (Shannon, 1948) which quantifies the amount of information contained in the signal. The spectral entropy SpEn (Inouye et al., 1991) applies the same equation but to the information contained in the frequency representation of the signal. The sample entropy SampEn (Richman and Moorman, 2000) is derived from the approximate entropy (Pincus et al., 1991) a method closely related to the Kolmogorov entropy and characterizing the rate of generation of new information. SampEn is used for Alzheimer patients assessment (Gomez et al., 2007) and was included in the features used for seizure detection algorithm (Aarabi et al., 2009). The permutation entropy permH (Bandt and Pompe, 2002) was developed as a fast and robust measure of complexity which, in known chaotic systems, behaves similarly to the Lyapunov exponents. It was used as a measure of sedation (Olofsen et al., 2008; Li et al., 2008) and for detection of a preictal state (Bruzzo et al., 2008; Ouyang et al., 2010).

All procedures were implemented in Matlab, except MP which was programmed in C. Ictal changes are highly variable among patients, therefore we opted to apply non-parametric statistical methods to analyze the change between the four periods. For each measure and each region, we tested with a one-way ANOVA on ranks for paired data (Friedman's test) if changes in levels were significantly modified between the four periods. Post-hoc testing was done using the paired sign-rank Wilcoxon test between adjacent periods (P2 versus P1, P1 versus S1 and S1 versus S2) and corrected for repetition ($p=0.05/2=0.025$). A comparison done by pooling all seizures together was also done to assess overall efficiency of each measure in typical monitoring settings.

3-Results

Table 1 includes the results of the Friedman analysis for all measures and all groups. Table 2 includes the results of the sign-rank paired tests. There is no significant difference between any of the P2-P1 comparisons for any of the measures and any of the groups. This confirms the relative stability of the preictal periods and reliability of the baseline periods used as the reference for normalization. Onset changes (P1-S1) are shown in the upper part of Table 2. Later changes (S1-S2) are shown in the lower part of Table 2. Figure 2, 3 and 4 only include the P1-S1 comparison.

Paired testing shows significant increases in signal power P between P1 and S1 periods for the MT group ($p=0.02$). Changes for UDT do not reach significance ($p=0.04$). For the frequency edge, only the MT and UDT groups show changes in median values. The frequency edge is significantly increased for MT ($p<0.001$) between P1 and S1, but not between S1 and S2. Changes for UDT are not significant for P1 versus S1 ($p=0.08$) nor for S1 versus S2 ($p=0.05$). Neither spectral power in the delta band [0–4Hz] or theta band [4–8Hz] show any significant changes across the four periods. Large increases for individuals patients are seen, especially in the theta band for the MT group, as reflected in the boxplot extent (Figure 2). Those increases however are not seen consistently across all patients.

Changes in the alpha band [8–12Hz] are mostly restricted to the MT group. Even though increases are seen starting between P1 and S1, only the S1–S2 difference reaches significance ($p<0.01$). A similar pattern is seen for the beta band [12–30Hz], but with a significant increase between P1 and S1 ($p<0.01$) and between S1 and S2 ($p=0.02$). No other groups exhibit consistent changes for either the alpha or beta band. The gamma band defined

here between 30 and 58Hz shows significant changes for all groups. Paired testing shows the S1-P1 differences to be significant for the MT ($p<0.01$) and NeoXT groups ($p=0.001$) but, due to multiple comparison correction, not UDT ($p=0.04$). Due to the sample size, the results for NeoT do not reach significance either ($p=0.06$). However, this is the lowest p value that can be obtained for a Wilcoxon test on such small sample ($N=5$) when all differences are the same sign and can be interpreted as a trend towards significance under those conditions.

High-frequency bands HF_{125} [62–125Hz] and HF_{300} [125–300Hz] also show significant differences in the median of the periods. For the lower band HF_{125} , the differences are between P1 and S1 for MT ($p=0.004$), NeoT ($p=0.06$), NeoXT ($p<0.001$), and UDT ($p=0.008$). For the upper band HF_{300} , the differences are between P1 and S1 for MT ($p=0.02$), NeoT ($p=0.06$), NeoXT ($p=0.009$) and also between S1 and S2 for MT ($p=0.02$). UDT differences are not significant in the post-hoc testing $p=0.04$ for S1-P1. For HF_{300} , one outlier in the NeoT group is omitted from the graph for the plot to remain readable.

The Friedman tests for GAD show significant differences between the medians for all regions. P1 versus S1 comparisons are significant for MT ($p<0.001$), NeoT ($p=0.06$), NeoXT ($p=0.01$) and UDT ($p=0.008$) groups. An increase is also shown between S1 and S2 for the MT group ($p=0.002$).

Differences in medians for C_{JS} are restricted to MT and UDT groups. However in post hoc multi comparison analysis no difference reaches the threshold for significance between P1 and S1 (MT: $p=0.08$; UDT: $p=0.1$). It should be noted that C_{JS} values decrease during ictal onset. Higuchi fractal dimension HFD shows a difference between medians for NeoXT and UDT groups. Those changes are for the ictal onset (P1 versus S1) for NeoXT ($p=0.02$) and UDT ($p=0.008$). The third Hjorth parameter, the complexity, is unchanged for NeoT and UDT, but reveals decreases in complexity between P1 and S1 for MT ($p=0.02$) and between S1 and S2 for NeoXT ($p=0.03$). Friedman tests for LZC reveal changes for MT, NeoXT and UDT groups. Post-hoc testing shows LZC increases between P1 and S1 for MT ($p<0.001$), NeoXT ($p=0.01$) and UDT ($p=0.008$).

Computation of the ShEn ratio was impossible for 15 seizures due to the lack of variability in the baseline period. The ratio would be infinite for reference period with no standard deviation. No single patient was dropped due to the removal of those 15 seizures (for ShEn only).

ShEn changes occurred only between the S1 and S2 periods. SpEn changes are only significant for the MT group between P1 and S1 periods ($p=0.004$) showing an increase at the onset of partial seizures. SampEn exhibits increases for all regions except NeoT. Increases are between P1 and S1 periods for MT ($p=0.002$) and NeoXT ($p=0.01$). Although Friedman test for UDT is significant, the post-hoc analysis does not reveal significant change in our comparison design (UDT: $p=0.05$). No difference is detected between ictal periods S1 and S2. PermH changes are only significant for MT and only later in the seizure for the S1 versus S2 comparison ($p=0.02$) showing a decrease in permutation entropy.

To assess how these differences observed for each group compare to results for individual seizures, the overall number of seizure for all patients with either increases or decreases relative to the baseline level were compared for each measure (Table 3). We counted the total number of seizure with changes (increase or decrease) between the periods P1 and S1 which exceed one standard deviation (T_1) and three standard deviations (T_3) of the baseline period I_{c0} . Here variations within patients are not taken into account, meaning for the same patient one seizure can exhibit a decrease in that measure for example and another seizure can exhibit an increase in that same measure. We also pool together all groups MT, NeoT,

NeoXT and UDT. Our intent here is to illustrate the potential discriminative power of these measures regardless of the region of seizure onset. ShEn was included in this analysis but with the caveat that the total number of seizures for ShEn is 15 less than for the other measures due to the discarded seizures mentioned above. Figure 5 shows the total number of seizures T_1 (dark colored bars) and T_3 (light colored bars). Large bars, positive or negative, indicate the ability of the measure to distinguish rapidly the onset of partial seizures from the baseline (inter-ictal). For the spectral-based measures, the number of seizures with positive and negative changes at the onset is linked to the frequency band considered. The lowest band δ exhibits slightly more negative changes than positive ones, while the γ and HF_{125} bands show almost exclusively increases at onset. For entropy measures, PermH shows that a large proportion of seizures features a decrease in permutation entropy early on in the seizure. Shannon entropy appears to be the least effective of the entropy measures to assess onset changes. Spectral entropy and sample entropy have similar efficiency. For the complexity measures, Hjorth complexity was the least able to measure changes at seizure onset, despite a large number of seizure T_1 showing Hjorth decreases, those changes remain modest in amplitude. The large HFD bars indicate that Higuchi fractal dimension often changes at the onset of a partial seizure but that the direction of those changes can be either an increase or a decrease. GAD is the measure showing the largest number of seizures (Figure 5) with changes greater than one and three baseline standard deviations.

4-Discussion

The onset of partial seizures, whether from scalp or intracranial ictal recordings, is traditionally described in terms of changes in rhythmic activity (frequency) and changes in amplitude. As we gain increased appreciation of the dynamical signal changes that occur during partial seizure evolution, it is appropriate to begin to extend assessment of seizure onset beyond these traditional methods. The systematic analyses presented here on a large number of ictal intracranial recordings represent the largest comparative application of various univariate methods (including measures of entropy and complexity) to the early period of partial seizure onset. The goal is to provide insight into the relative merits and potential of these various methods.

For mesial onset seizures, significant changes between preictal and ictal levels were observed for signal power (P), frequency edge (F_e), beta and all frequency bands upward of beta, Gabor atom density (GAD), Hjorth complexity, Lempel-Ziv complexity (LZC), spectral entropy (SpEn) and sample entropy (SampEn). It is important to note that the power in the lower frequency bands delta, theta and alpha did not significantly change at the onset of partial seizures. This apparent contradiction to the common descriptor of partial seizure onset in mesial temporal lobe epilepsy patients can be explained by two factors. First, the activity in the lower bands of the EEG may not be specific enough. Even if theta onset patterns are commonly observed, theta activity is not pathological and is commonly observed during sleep and other normal physiologic states. Second, and likely, the theta build up pattern often described is a process that takes time and is not represented in the early seizure epochs analyzed here. Wendling and Chauvel reported spectral changes clearly showing a higher frequency onset (beta range) several seconds before the significant build up of theta activity (Wendling and Chauvel, 2008). They also reported that fast oscillations above gamma are not usually observed in the mesial onset seizures. Observation of high-frequency oscillations (HFO) in the 100–500Hz range were reported in mesial onset seizures as well as neocortical onset seizures (Bragin et al., 1999; Jirsch et al., 2006). The ubiquity of these HFO at the onset of partial seizures is still under study to determine whether or not they are markers of the epileptogenic onset zone, but the significance of the increases in all bands above and including gamma that we observed here is consistent with these reports. The alpha band changes show progressive build-up occurring later in the seizure.

This significant increase in all frequency bands above and including beta is contributing to the changes in the F_c and SpEn. Both LZC and the SampEn which measures the occurrence of new patterns in time series show increases at the onset of those higher frequency components. Studies of the effect of spectral bandwidth on LZC and the approximate entropy (ApEn) showed that both measures increase with the spectral bandwidth of the EEG signal (Aboy et al., 2006; Ferenets et al., 2006). This makes it difficult to distinguish, without surrogate analysis, the relative influence of changes in spectral bandwidth and signal complexity. The permutation entropy (PermH) also exhibits changes but only later in the seizures.

For the neocortical temporal onset seizures, changes were somewhat harder to assess due to the small sample size and therefore we could only assess changes at a significance level of 0.06. The most interesting patterns are that the high-frequency bands gamma, HF_{125} and HF_{300} show significant increases as GAD does. These changes in high-frequency bands do not translate to changes in power or frequency edge nor to changes in any of the entropy or other complexity measures.

Neocortical extratemporal onset seizures show similar effects in the high-frequency domain ranging from gamma to the upper 300Hz band similar to seizures originating from other cerebral regions. GAD signal complexity shows increases reinforcing the apparent association between GAD and high-frequency content. The algorithmic complexity LZC, the fractal dimension HFD and the sample entropy SampEn are also increased.

The last group (UDT) was a mixed group of patients and seizures traditionally not included in analysis due to their unlocalized nature. We restate here that our purpose in including this group was to investigate all types of seizure onsets, especially when the clinical diagnosis is only that of partial seizures, to assess the potential of those measures to provide additional potentially beneficial information in these challenging patients. Despite the potential heterogeneity of the group, several measures were significantly modified at the onset of those seizures. In the spectral domain, only one band, HF_{125} showed significant increases with ictal onset. GAD complexity also featured a consistent increase. Two other complexity measures (HFD and LZC) exhibited significant increases at onset. None of the entropies showed any significant changes.

The comparison of methods done by assessing the number of seizures with changes in levels greater than the baseline standard deviation present a different picture of the changes occurring at seizure onset. Even measures such as the power in the delta band or alpha band which do not exhibit any significant changes when grouped by patient and region reveal that a large number of seizures still feature increases when considered individually. Of all measures, GAD remains the most consistently able to assess these changes, closely followed by the high-frequency power bands, F_c , SampEn, SpEn and LZC. The ratio of seizure featuring increases or decreases gives us an indicator of the relative behavior of these measures at ictal onset. GAD exhibits a consistent increase of signal complexity in the vast majority of seizures, while HFD, for example, indicates that the fractal dimension of these same seizures might not always produce changes that parallel the signal complexity. A combination of indicators might give an even better idea of the dynamic changes occurring early in a seizure.

The increase for all regions of the power bands above gamma is a very positive indicator of the importance of the high-frequency components of the EEG signal in the assessment of early onset of partial seizures. The role of the high-frequency component is also probably a factor in the increase of GAD complexity across all regions. It also highlights the ability of the GAD measure to primarily detect the increases in the number of atoms of the time-

frequency decomposition in the high-frequency portion of the spectrum. The potential for GAD as a indicator of early seizure onset has been recently reported (Jouny et al., 2010).

LZC proved to be a good indicator of early seizure onset. It measures occurrence of new patterns in the sequence of EEG values and therefore it seems logical that it would be exhibiting increasing values as the ictal EEG contains additional high-frequency components that increase the irregularity of the EEG traces. Two preliminary studies (Radhakrishnan and Gangadhar, 1998; Abasolo et al., 2007) indicate increased LZC during seizures. Hu et al. reported large decreases of LZC post-ictally but did not provide information on the ictal behavior itself (Hu et al., 2006).

The Higuchi fractal dimension (HFD) is a strong indicator when considering the entire pool of all the seizures, however, the results of the analysis per region reveal a sensitivity only to neocortical extratemporal onset seizures and not mesial onset ones. This difference is actually an interesting indicator of a possible means to differentiate mesial temporal onsets from neocortical onset seizures. Two studies reported increases in HFD during ictal events but both were inconclusive as to the general behavior of HFD (Paramanathan and Uthayakumar, 2008; Polychronaki et al., 2010).

While we found only a few studies using sample entropy (SampEn) in the analysis of ictal events, approximate entropy (ApEn) from which SampEn derives was studied somewhat more. Diambra et al. tested the use of ApEn on scalp recordings of epileptic patients (Diambra et al., 1999). Using only one preset electrode F8 for all patients, they reported a decrease in ApEn during epileptic activity. Srinivasan et al. used ApEn to feed an artificial neural network to differentiate normal from epileptic recordings, indicating a trend for lower ApEn values for epileptic recordings (Srinivasan et al., 2007). A comparative study of ApEn and LZC showed consistent increases with the occurrence of ictal events but only analyzed one patient (Abasolo et al., 2007). A similar study comparing LZC and ApEn showed that both measures varied during the ictal event with increases at onset but decreases in the middle of the event (Radhakrishnan and Gangadhar, 1998). Considering the preliminary assessment of those studies, a clear pattern of ApEn (and SampEn) behavior during ictal onset could not be ascertained until now. Here we found that SampEn shows predominantly increases at the early onset of partial seizures and for mesial onset seizures. Second to GAD in total number of seizures with early changes greater than one standard deviation, SampEn is a very interesting potential source of information that deserves to be investigated further.

Permutation entropy (PermH) consistently reveals changes later in the seizure, although its relatively high score in the analysis of pooled seizures contrasts with analyses of seizures grouped by region. The only other large scale study of PermH on seizure dynamics is an animal study (Li et al., 2007) which reports decreases of PermH during absence seizure onset in genetic absence epileptic rats. A study in humans seems to suggest also a decrease of PermH in the periods leading to an ictal onset (Bruzzo et al., 2008). However this study includes only 3 patients and as all seizures occur during sleep stage transition, the authors themselves acknowledge the possibility that the seizure detections were merely coincidental to the state transition. C_{JS} did not reveal any significant changes in the region of onset analysis. However C_{JS} exhibits frequent changes at individual seizure onset but those changes do not appear consistent within each onset region. The Plastino et al. study of wavelet-based complexity C_{LMC} which was the precursor of C_{JS} showed increase in complexity (Plastino and Rosso, 2005) but only on a single seizure. Hjorth complexity showed relatively poor efficiency to track early ictal changes. Despite its sensitivity to spectral bandwidth, it was not able to measure significant changes except for the mesial onset seizures. Shannon entropy (ShEn) and spectral entropy (SpEn) were unable to reveal effects apart from the mesial group.

All the measures were implemented with the smallest set of parameters possible to avoid any training effect on our dataset during the implementation. Investigation of the effects of the parameters of the measures to assess whether some detection parameters would be more beneficial for some specific onset types (mesial versus neocortical) remains to be done.

Summary of measures relative effectiveness

Due to the large number of measures, to attempt to summarize the relative advantages of each measure, we constructed the following illustration (Fig. 6). We selected the two groups with the largest number of patients (MT and NeoXT), and for each type of measures (spectral, complexity and entropy), we represented each measure with an ellipse which x and y positions are calculated as the mean increase for that measure at the onset of each seizure and averaged over all MT seizures (x-axis) and all NeoXT onset seizures (y-axis). As each measure is expressed relative to the baseline standard deviation (see Methods), the axis have no unit. Each ellipse spread corresponding to the standard deviation over the respective group. A root square transformation was applied to the data for all the measures to constrain the range of the ellipsoids and allow a visual comparison. A zero value indicates a measure for which the value does not change between preictal period P1 and ictal period S1. A value of 2 indicates that the measure is increased between P1 and S1 periods by an average of 4 times (2^2) the baseline standard deviation. A negative value indicates that the measure decrease between P1 and S1 periods. In this representation, the intersection of the x and y axis indicates a measure which would not be sensitive to either MT onset seizures or NeoXT onset seizures. The most likely measure able to detect seizure onset would be one for which the corresponding ellipsoid is the furthest away from the axis (larger increase), and the one that possesses the smallest spread (most consistent). It is also important to realize that a measure on the diagonal would be the best detector for either MT or NeoXT onset seizures, but also the least able to distinguish the onset region. In each group of measures for example, HF60, SampEn and GAD are the most able detectors for seizure onset regardless of the onset region. At the same time, the increase observed at onset for each of those measures will not be any indicator of the region. HFD which on the other hand sits right on the y-axis is unlikely to be able to detect MT onset seizures, but is an indicator of a NeoXT onset seizure.

The spectral panel (Fig. 6A) shows the relative efficiency of each frequency band where the lower frequency bands up to beta seems more adequate to detect MT onset seizures, while higher frequency bands are evenly able to detect MT or NeoXT onset seizures. While the position of the high frequency band ellipsoids indicates the highest likelihood of being able to detect seizure onsets, their larger size also indicates the largest variability - and therefore smallest consistency of all the measures. As expected, the total power ellipsoid sits approximately at the gravity center of the ones for specific bands, highlighting the continuum of position for each frequency band ellipsoids in a counter clockwise arrangement around the ellipsoid for the total power P. The arrangement of the ellipsoid with their frequencies is consistent with selection of beta frequency as a primary indicator for the onset of mesial onset seizures as used in detection methods (Osorio et al., 1998).

The entropy panel (Fig. 6B) shows the mere identical results of ShEn and SpEn. SampEn is the most likely measure to be able to detect either type of seizure onset. While PermH position in a different quadrant indicates its ability to differentiate seizure onset region. Given that PermH assesses the occurrence of self-similarity in the EEG patterns, it also hints at specific differences in ictal EEG patterns between mesial regions and neocortical regions.

The complexity panel (Fig. 6C) shows the low sensitivity of Hjorth and C_{JS} measures to detect either type of ictal onsets. Both measures also are inverted compared to other complexity measures, showing decreases in complexity during ictal onset. C_{JS} is a

constructed measure designed to tend towards zero for both highly regular and highly irregular patterns, and its evolution during ictal event were never investigated apart from a single seizure study (Plastino et al., 2005). Hjorth complexity which measures the spread of the frequency composition is potentially reflecting the appearance of a more dominant frequency in the EEG. LZC position indicates a slightly better detection ability than delta band power, but remains less effective than SampEn and GAD. As mentioned before, HFD positioning highlights its use for differentiation of seizure onset regions.

5 - Conclusions

This extensive analysis of a large number of currently employed complexity and entropy measures is a first step in investigating the breadth of changes that occur at the onset of partial seizures. This study highlights some of the common changes that might affect many different measures. Although these measures have been designed to assess different properties, real world signals are always composed of concomitant changes (e.g. spectral shift with a change in entropy). The classification of the measures (spectral-based, entropy or complexity) does not correlate with the ability of the measure to assess ictal onset changes.

However these 18 measures are unlikely to measure 18 different individual properties of the signal. From their definition, we could expect that some of the measures would present similar patterns of behavior; for example both Sample entropy and LZC measures the occurrence of new patterns in the signal. Similarly spectral entropy and frequency edge are directly affected by any changes in spectral composition of the signal. In both cases, correlations of these measures are expected as both assess the same phenomenon, although using a different formulation. We can conclude that several of the measures we evaluated are sensitive to the occurrence of new EEG patterns and those patterns at the onset of partial seizures often involve high frequency components. Power in the high frequency bands is confirmed here to be a crucial indicator of the early sign of seizure onset. While power in the beta band (12–30Hz) is the most likely to detect MT onset seizures, spectral components above that frequency are likely markers for both MT and NeoXT onset seizures. The difference in the changes detected by the Gabor atom density and the Higuchi fractal dimension or sample entropy and permutation entropy underscore the potential for these measures and their combination to help discern onset region and characterize early ictal onset patterns in a multidimensional fashion.

Further analysis of sensitivity, specificity (including false positive rate) and detection delay is necessary to provide a complete assessment of the potential of those measures, however the characterization of early seizure onset is a critical step in the implementation of modern responsive devices designed to detect and intervene early in seizure evolution. The choice of parameter for the measures was mostly based on the existing literature, further study of the parameter selection process could potentially reveal new insights on way to increase sensitivity by fine tuning these parameters. Multichannel analysis (Korzeniewska et al., 2009) and studies of functional network topology (Schindler et al., 2007, 2008) are other potential paths that can complement our understandings of network dynamics and provide additional indicators of seizure onset at the very early stage of seizure evolution.

6 - Significance

The combination of several measures is potentially an important way to improve the efficiency of seizure onset detection. Yet selection of the methods as spectral based, complexity based or entropy based is not predictive of the efficiency of the method to detect early seizure onset. Although current detection methods often rely on a set of several

features, no large scale study has yet attempted to integrate complexity and entropy measures to the extend presented here. It is interesting to complement the current clinical assessment of ictal EEG changes with these new approaches. These measures of EEG quantification can offer new ways to understand and redefine ictal onset, with knowledge of the specificity of certain measures to assess region of onset, while others offer consistency of detection regardless of the region.

Highlights

- This study compares the relative ability of spectral-based measures, entropy measures and complexity measures to detect early seizure onset.
- Gabor atom density, Higuchi fractal dimension, Lempel-Ziv complexity, sample entropy and power in the high-frequency bands are the most reliable measures to assess ictal activity within 8 seconds of the electrographical onset.
- The best performing measures for early seizure detection are selected methods from spectral, entropy, and complexity domain, highlighting the need for a multimodal approach to understanding partial seizure onsets to improve seizure detection efficiency.

Acknowledgments

Support provided by NIH R01 NS48222.

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Appendix A. Methods and parameters

We used the following common notations for all methods.

x : input signal

Y : FFT transform of x

W_L : Window length. This is a common parameter for all analyses

W_S : Window shift. This is also a common parameter for all analyses

Number and values of each specific parameter for each method is indicated in parenthesis.

Signal power – P

Signal power in the window considered is the sum of the signal amplitude squared divided by the window length. There is no parameter for its evaluation.

$$P = \frac{1}{W_L} \sum_0^{W_L} |x|^2$$

Frequency edge (80%) - F_e

Frequency edge F_e at 80% is defined as the frequency for which 80% of the total power of the signal is contained in frequencies lower than the frequency edge.

$$\frac{\sum_0^{F_e} |Y|^2}{\sum_0^{-\infty} |Y|^2} = 80/100$$

Typical percentage studied range from 80 to 95%. The measure sensitivity depends on having the value obtained for F_e in the range of the activity changes that you want to observe. Therefore at 80%, we target F_e to have maximum sensitivity for changes in spectral composition towards the upper end of the EEG spectrum. The threshold (80%) is the only parameter of the method.

Power in frequency bands

Power in the frequency band [f₁ f₂] is computed as:

$$P_{[f_1, f_2]} = \sum_{f=f_1}^{f_2} |Y_f| \cdot \Delta f$$

The bands selected were δ : [0–4Hz[, θ : [4–8Hz[, α : [8–12Hz[, β : [12–30Hz[, γ : [30–58Hz[, HF₁₂₅ : [62–125Hz[and HF₃₀₀ : [125–300Hz]. Lower bands limits were based on traditional EEG band definition used for sleep and wakefulness studies. However higher bands do not have a commonly accepted definition. In particular limit between the last two upper bands was chosen at 125Hz to split the 60–300Hz range. The lower and upper limit of the frequency band studied are the only two parameters of the method.

Gabor atom density – GAD

GAD is computed from the matching pursuit (MP) decomposition as the density of atoms obtained from MP divided by the size of the time-frequency domain considered Δt , Δf where Δt and Δf are the respective time and frequency size of the window analyzed. MP is run with an energy threshold of $10\mu V^2$. GAD was shown to scale linearly with the energy threshold as long as the threshold was sufficient low, and well below the coherence threshold originally proposed by Mallat. If m atoms have been produced by MP over a window of N points, GAD can be expressed as:

$$GAD = \frac{m}{\Delta t, \Delta f} = \frac{2m}{N}$$

The energy threshold of $10\mu V^2$ is the only parameter of the method.

Entropic non-triviality measure - C_{JS}

If the signal x has a amplitude distribution $\vec{p}$, the non-triviality entropic measure is defined as the product of the entropy H of the signal and a measure of disequilibrium Q_{JS} based on the Jensen-Shannon divergence:

$$C_{JS} = H[\vec{P}] \cdot Q_{JS}[\vec{P}]$$

with:

$$Q_{JS}[\vec{P}] = Q_0^{(JS)} \cdot J^{\frac{1}{2}, \frac{1}{2}}[\vec{P}, \vec{P}_e]$$

where $\vec{P}_e$ is the uniform distribution, Q_0 is the normalization constant and is the inverse of the maximum possible value for J (obtained when $\vec{P}$ is a Dirac distribution). The divergence J for two distributions P_1 and P_2 is defined as:

$$J^{\pi_1/\pi_2}[\vec{P}_{(1)}, \vec{P}_{(2)}] = H[\pi_1 \vec{P}_{(1)} + \pi_2 \vec{P}_{(2)}] - \pi_1 H[\vec{P}_{(1)}] - \pi_2 H[\vec{P}_{(2)}]$$

with π_1 and π_2 are the respective weight for each distribution. The entropic non-triviality measure does not require any parameter.

Higuchi fractal dimension – HFD

The Higuchi fractal dimension is computed by creating new times series from the original signal using various delays m and periods k for sampling. The length of the curve of each serie is then computed:

$$L_m(k) = \left\{ \left(\sum_{t=1}^{\lfloor \frac{N-m}{k} \rfloor} |x(m+tk) - x(m+(t-1)k)| \right), \frac{N-1}{\lfloor \frac{N-m}{k} \rfloor}, k \right\} / k$$

The average value of the length of curve $\langle L(k) \rangle$ is proportional to k^{-HFD} if the curve is fractal. HFD is the slope of the linear regression model using least square estimator to fit the points of the logarithm of the average curve length versus the logarithm of k . m dynamically goes from 1 to k . Report of a study for optimal maximum value for k when analyzing ECoG in animals (Spasic et al., 2006) shows that as long as k_{max} is large enough ($k_{max} > 8$), HFD estimates are monotonously increasing with k . Based on our preliminary data, as k_{max} indicates the number of points available for the linear regression, a value of 30 was chosen a posteriori to be sufficient to provide a reliable estimator of the slope. k_{max} is the only parameter for the evaluation of HFD.

Hjorth complexity

Hjorth complexity is a measure of the root-mean square frequency spread. It is computed as:

$$C_{Hjorth} = \sqrt{\sigma_2^2 / \sigma_1^2 - \sigma_1^2 / \sigma_0^2}$$

where σ_n^2 are the variances of the derivative of order n of the signal x . There is no parameter required for this measure.

Lempel-Ziv complexity – LZC

The algorithm to compute LZC is described in Kaspar et al. (1987). There is no equation to compute LZC, it is obtained by an iterative procedure of identification of patterns in the binary string S created after a prefiltering of the original sequence which transform the original signal into a coded string with a limited vocabulary. Several option of prefiltering exist, the most commonly used is done using a median filter for which all values above median are coded as 1 and all values below median are coded 0 (Aboy et al., 2006). Each element S_{r+1} is checked against the vocabulary of string elements already processed S_r . If the element exists already, the procedure tests if the combination $S_{r+1}S_{r+2}$ is also already part of S_r , and continue until the new sub chain is not found in the vocabulary. The new chain is therefore added to the vocabulary, and the number C of production steps to insert new chain is the base for the measure of complexity. LZC is computed as C normalized by $n/\log_2 n$. There is no numeric parameter to this measure, although the choice of pre-filtering method can be considered as a parameter of the measure. We chose to use the median pre-filtering to create the binary string.

Shannon entropy – ShEn

Shannon entropy is often called a measure of uncertainty. This entropy represents the degree to which the probability of the system is spread out over different possible states of the system – here the states are the possible amplitudes of the signal. Entropy is computed from the distribution of the signal amplitude.

$$H = - \sum_{i=1}^n p(x_i) \ln(p(x_i)) \quad \text{where } p_i = \frac{|x_i|}{\sum |x_i|}$$

There is no parameter required to compute Shannon entropy.

Spectral entropy – SpEn

Spectral entropy is a particular case of Shannon entropy where the distribution p is the normalized power spectrum of the signal. The states here are the different amplitude levels in each frequency bands.

$$p_i = \frac{|Y_i|}{\sum |Y_i|}$$

There is no parameter required to compute the spectral entropy.

Sample entropy – SampEn

SampEn is also estimated by an iterative procedure. SampEn is the negative natural logarithm of the conditional probability that two sample series having repeated themselves within a tolerance r for m points, will also repeat itself for $m+1$ points, without allowing self-matches. SampEn evaluation required two parameters which were the matching length $m=2$ and the tolerance $r=0.2$. These values are commonly used for SampEn estimation although no clear guide exists for their selection. Lake et al. did a small study of the optimization of m and r which revealed similar values ($m=3$, $r=0.2$) for neonatal heart data (Lake et al, 2002).

Permutation entropy – PermH

Permutation entropy is defined as the sum over all $n!$ permutations π of order n of the probability of the occurrence of each permutation multiplied by the natural logarithm of that probability.

$$PermH_n = - \sum_{\pi} p(\pi), \log p(\pi)$$

A permutation of order n is the relative position of n consecutive elements of x . PermH order n is the only parameter for this measure. Based on results and comments by Bandt (Bandt and Pompe, 2002) that “since the method is extremely fast and robust, it seems preferable when there are huge data sets and no time for preprocessing and fine-tuning of parameters”, order n was fixed at 4.

Figure 1.

EEG signal and corresponding values of three measures (HFD, C_{JS} , Gamma) over a 40s window around the electrographical onset of the seizure. Each of the four periods P2, P1, S1 and S2 contain 5 data points (marked with dots) spaced over 4.096s. As each point is computed over a window of analysis W_L of 4.096s, each period reflects activity over timeframe of 8.192s as shown by the horizontal bars over the EEG. Points around time zero are excluded so P1 and S1 periods have no overlap. Z-score is a normalization technique (subtract mean and divide by the standard deviation) and is only use for representation purpose in this figure.

Figure 2.

Summary of difference P1-S1 for the signal power, frequency edge and all the spectral bands for each patient group MT, NeoT, NeoXT and UDT. Each boxplot shows the median as the black marker inside the box. Each box extends from the 25 percentile to the 75 percentile. Sign + indicates the outliers. Y-axis scale is without unit and represents the difference between S1 and P1 levels in number of baseline standard deviation. One extreme outlier was omitted for HF₃₀₀ plot of NeoT group.

Figure 3. Summary of difference P1-S1 for the complexity measures (GAD, C_{JS} , HFD, Hjorth, LZC) for each patient group MT, NeoT, NeoXT and UDT. Each boxplot shows the median as the black marker inside the box. Each box extends from the 25 percentile to the 75 percentile. Sign + indicates the outliers. Y-axis scale is without unit and represents the number of baseline standard deviation.

Figure 4. Summary of difference P1-S1 for the Shannon entropy (ShEn), spectral entropy (SpEn), sample entropy (SampEn) and permutation entropy (PermH) for each patient group MT, NeoT, NeoXT and UDT. Each boxplot shows the median as the black marker inside the box. Each box extends from the 25 percentile to the 75 percentile. Sign + indicates the outliers. Y-axis scale is without unit and represents the number of baseline standard deviation.

Figure 5.

Classification of the measures by the number of seizures with increase (blue) or decrease (orange) at seizure onset (S1-P1). Light colored bars indicate number of seizure with changes greater than three baseline standard deviation. Dark colored bars indicate number of seizure with changes greater than one baseline standard deviation. Total number of seizures = 331. Spectral measures are ordered by frequency for readability. Entropy and complexity measures are ordered by the number of seizure with positive changes at onset.

Figure 6.

Illustration of the relative likelihood of the measures to provide critical information during early seizure onset (see in text for further details). Spectral measures (A), entropy measures (B) and complexity measures (C) are represented as ellipsoids whose position (and spread) represents the mean (standard deviation) of the early ictal change between S1-P1 periods averaged over all MT onset seizures (x-axis) and NeoXT onset seizures (y-axis). Ellipsoid outlines are shown for all measures on the three panels for a visual comparison of the relative position of each measure. The frequency edge (Fe) ellipsoid which overlapped almost completely with the delta one was omitted for clarity. Ellipsoid on the diagonal indicates measures which exhibit similar changes at onset regardless of the seizure region.

Ellipsoids on either side of the diagonal indicate an affinity to detect seizure for that specific region. Measures for which the ellipsoid is the furthest from the origin have the largest potential to exhibit large increases compared to baseline during the first 8 seconds after the electrographical onset of a seizure.

Table 1

Summary of effects by Friedman analysis.

Friedman	P	Fe	δ	θ	α	β	γ	HF ₁₂₅	HF ₃₀₀	GAD	C _{JS}	HFD	Hjorth	LZC	ShEn	SpEn	SampEn	PermH
MT	*	*			*	*	*	*	*	*	*	*	*	*	*	*	*	*
NeoT						*	*	*	*	*								
NeoXT						*	*	*	*	*	*	*	*	*	*		*	*
UDT	*	*				*	*	*	*	*	*	*	*	*	*		*	*

Stars (*) indicate that the hypothesis H0 of equal periods is rejected and there is significant changes between the four periods (P2, P1, S1, S2) at the significance level $p=0.05$.

P: total power; Fe: Frequency edge; δ : delta band; θ : theta band; α : alpha band; β : beta band; γ : gamma band; HF125 [62–125Hz] band; HF300 [125–300Hz] band; GAD: Gabor atom density; CJS: entropic non-triviality measure; HFD: Higuchi fractal dimension; Hjorth: Hjorth complexity; LZC: Lempel-Ziv complexity; ShEn: Shannon entropy; SpEn: spectral entropy; SampEn: sample entropy; PermH: permutation entropy.

Table 2

Summary of effects for post-hoc testing between preictal period P1 and ictal period S1 (upper) and between ictal periods S1 and S2 (lower).

P1-S1	P	Fe	δ	θ	α	β	γ	HF ₁₂₅	HF ₃₀₀	GAD	C _{JS}	HFD	Hjorth	LZC	ShEn	SpEn	SampEn	PermH
MT	*	*				*	*	*	*	*			*	*	*	*	*	*
NeoT						+	+	+	+	+								
NeoXT						*	*	*	*	*		*		*			*	*
UDT							*	*	*	*		*		*				
S1-S2	P	Fe	δ	θ	α	β	γ	HF ₁₂₅	HF ₃₀₀	GAD	C _{JS}	HFD	Hjorth	LZC	ShEn	SpEn	SampEn	PermH
MT					*	*	*	*		*					*			*
NeoT																	+	
NeoXT																		*
UDT																		

Stars (*) indicate significance of post-hoc sign rank test between periods at $p < 0.025$.

Plus signs (+) indicate $p = 0.06$ which is the minimum for the NeoT group due to the small sample size.

P: total power; Fe: Frequency edge; δ : delta band; θ : theta band; α : alpha band; β : beta band; γ : gamma band; HF125 [62–125Hz] band; HF300 [125–300Hz] band; GAD: Gabor atom density; CJS: entropic non-triviality measure; HFD: Higuchi fractal dimension; Hjorth: Hjorth complexity; LZC: Lempel-Ziv complexity; ShEn: Shannon entropy; SpEn: spectral entropy; SampEn: sample entropy; PermH: permutation entropy.

Table 3

Summary of number of seizures with P1-S1 differences.

	Inc ₁	Dec ₁	T ₁	Inc ₃	Dec ₃	T ₃
P	150	82	232	80	28	108
F_e	248	29	277	200	7	207
δ	69	107	176	41	27	68
θ	159	82	241	121	19	140
α	169	67	236	129	19	148
β	195	41	236	161	13	174
γ	254	25	279	213	9	222
HF₁₂₅	251	25	276	211	8	219
HF₃₀₀	218	31	249	158	13	171
PermH	70	198	268	51	131	182
ShEn	145	77	222	70	30	100
SpEn	231	47	278	158	15	173
SampEn	243	39	282	181	8	189
Hjorth	29	141	170	7	17	24
C_{JS}	75	157	232	25	67	92
HFD	154	127	281	115	57	172
LZC	232	29	261	148	5	153
GAD	269	22	291	218	10	228

Inc₁ and Inc₃ are the number of seizures with increases larger than one, respectively three, baseline standard deviation. Dec₁ and Dec₃ are the number of seizures with decreases larger than one, respectively three, baseline standard deviation. T indicates the total number of seizures Inc+Dec.

P: total power; F_e: Frequency edge; δ:delta band; θ:theta band; α:alpha band; β:beta band; γ:gamma band; HF₁₂₅ [62–125Hz] band; HF₃₀₀ [125–300Hz] band; GAD: Gabor atom density; C_{JS} entropic non-triviality measure; HFD: Higuchi fractal dimension; Hjorth: Hjorth complexity; LZC: Lempel-Ziv complexity; ShEn: Shannon entropy; SpEn: spectral entropy; SampEn: sample entropy; PermH: permutation entropy.