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Mean phase coherence as a measure for phase synchronization and its application to the EEG of epilepsy patients

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Abstract

We apply the concept of *phase synchronization* of chaotic and/or noisy systems and the statistical distribution of the relative instantaneous phases to electroencephalograms (EEGs) recorded from patients with temporal lobe epilepsy. Using the *mean phase coherence* as a statistical measure for phase synchronization, we observe characteristic spatial and temporal shifts in synchronization that appear to be strongly related to pathological activity. In particular, we observe distinct differences in the degree of synchronization between recordings from seizure-free intervals and those before an impending seizure, indicating an altered state of brain dynamics prior to seizure activity. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

The present paper reports on the application of the concept of phase synchronization to biological time series of the brain electrical activity of epilepsy patients. In the past few years, synchronization phenomena in chaotic systems have attracted much attention in the field of nonlinear dynamics and have found applications in areas such as laser dynamics [1,2], solid state physics [3], electronics [4], biology [5], and communication [6]. As a specific type of synchronization, the concept of *phase synchronization* was introduced for coupled chaotic model systems by Rosenblum et al. [7] and has been confirmed experimentally [8]. Only recently this concept has been applied to biological time series such as heart beat and respiratory rate in humans [9–12] and the magneto-encephalogram of Parkinsonian patients [13].

Here, we investigate yet another kind of biological time series: the brain electrical activity of epilepsy patients. Due to the relatively high incidence (approximately 1% of the world population) of this disease, there has been much research on its underlying pathological mechanisms. In almost all of the theories on epileptogenesis commonly accepted today, pathological neuronal synchronization is considered to play a crucial role [14,15]. However, in medicine the term

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synchronization is mostly used in a rather intuitive way [16] and even in physics no unified definition has been established so far but instead a variety of definitions are in use depending on the system under investigation. On the one hand, no specific measure for synchronization has been introduced to epilepsy research up to now. On the other hand, discerning the synchronization of processes and events in the brain might offer the possibility of gathering deeper insight into the development of epileptic seizures. For these reasons, the quantitative investigation of spatial and temporal changes in synchronization related to epileptic activity appears to be a promising venture.

2. Phase synchronization in chaotic or noisy systems

The notion of synchronization was introduced to physics by Huygens [17] in the 17th century for two coupled frictionless harmonic oscillators. For this classical case, phase synchronization is usually defined as locking of the phases of two oscillators:

$$\varphi_{n,m} = n\phi_a(t) - m\phi_b(t) = \text{constant}, \tag{1}$$

where n and m are integers, ϕ_a and ϕ_b denote the phases of the oscillators, and $\varphi_{n,m}$ is defined as their *relative phase*. In order to investigate synchronization of chaotic systems, Rosenblum et al. [7] replaced this condition of *phase locking* by the weaker condition of *phase entrainment*:

$$|\varphi_{n,m}| = |n\phi_a(t) - m\phi_b(t)| < \text{constant}, \tag{2}$$

or by the even weaker condition of *frequency locking*:

$$\begin{aligned}\langle\omega_{n,m}\rangle &= n\langle\omega_a\rangle - m\langle\omega_b\rangle \\ &= n\left\langle\frac{\mathrm{d}\phi_a(t)}{\mathrm{d}t}\right\rangle - m\left\langle\frac{\mathrm{d}\phi_b(t)}{\mathrm{d}t}\right\rangle = 0,\end{aligned} \tag{3}$$

where $\langle\,\rangle$ denotes averaging over time, and $\omega_{n,m}$ the *relative frequency* of the systems. To investigate whether two systems show phase synchronization it is first of all necessary to know their phase variables $\phi_a(t)$ and $\phi_b(t)$. This is nontrivial for many nonlinear model systems and even more difficult when dealing with noisy time series of unknown origin. We therefore follow the *analytic signal* approach [18,19] to determine the *instantaneous phase* of an arbitrary signal $s(t)$:

$$\phi(t) = \arctan\frac{\tilde{s}(t)}{s(t)}, \tag{4}$$

where

$$\tilde{s}(t) = \frac{1}{\pi}\text{p.v.}\int_{-\infty}^{+\infty}\frac{s(\tau)}{t-\tau}\mathrm{d}\tau \tag{5}$$

is the *Hilbert transform*of the signal (p.v. denoting the Cauchy principal value).

Application of the convolution theorem turns (5) into

$$\tilde{s}(t) = -\mathrm{i}\,\mathrm{FT}^{-1}[\mathrm{FT}[s(t)]\,\mathrm{sign}(\omega)], \tag{6}$$

where FT denotes Fourier transformation and FT^{-1} inverse Fourier transformation, respectively. From this notation it becomes evident that the Hilbert transform performs a phase shift of the original signal by $\frac{1}{2}\pi$ in the frequency domain while the power spectrum remains unchanged [20].

It is important to note that the instantaneous phase as defined in Eq. (4) is restricted to the interval $[0, 2\pi]$ and has to be "unfolded" or "continuized" [21] (i.e. shifted by 2π whenever a 2π-phase-slip occurs) prior to taking its derivative (cf. Eq. (3)).

Using the relative frequency as a measure for synchronization, Rosenblum et al. [7] were able to show for the Rössler system [22] that coupled chaotic oscillators may phase-synchronize in the sense of Eq. (3) just as periodic oscillators do. However, when dealing with noisy or chaotic systems like periodically driven Lorenz systems [23] (where the chaotic amplitudes can affect the phase like noisy perturbations in the evolution of the system's trajectory), it turns out that the system's relative phase (i.e. the difference between the phase of the chaotic motion and the phase of the driving force) can more or less randomly exhibit rapid phase jumps with a length of 2π (a detailed discussion of this phenomenon is given in [24] and references therein). Due to these phase jumps, the relative frequency is strongly affected by noise which

makes it an inadequate measure for synchronization in noisy time series such as the EEG. To overcome this problem, we follow [11–13] in taking a more statistical point of view by analyzing the distribution of relative phase angles on the unit circle (i.e. the interval $[0, 2\pi]$): if the phases are locked during most of the time, a prominent peak will result in the phase histogram, and the effect of 2π-phase-jumps will no longer be predominant. One way of projecting the relative phases onto the interval $[0, 2\pi]$ is taking the (unfolded) relative phase modulo 2π. Alternatively, when using the analytic signal approach described above, application of a trigonometric addition theorem [20] renders the relative phase, for instance for $n = m = 1$,

$$\begin{aligned}\varphi_{1,1}(t) &= \phi_a(t) - \phi_b(t) \\ &= \arctan\frac{\tilde{s}_a(t)s_b(t) - s_a(t)\tilde{s}_b(t)}{s_a(t)s_b(t) + \tilde{s}_a(t)\tilde{s}_b(t)}\end{aligned} \tag{7}$$

naturally confined to the interval $[0, 2\pi]$.

In order to define an actual measure of synchronization, we use a concept similar to the *index based on conditional probability* proposed in [13]. Since our aim is to measure the synchronization between time series which are obtained from the same physiological system (i.e. the brain), we consider it most likely to encounter synchronization at a phase locking ratio of $n : m = 1 : 1$. Thus restricting ourselves to the case $n = m = 1$, we employ as a measure for synchronization the *mean phase coherence of an angular distribution* [25] defined as

$$R = \left| \frac{1}{N} \sum_{j=0}^{N-1} \mathrm{e}^{\mathrm{i}\varphi_{1,1}(j\Delta t)} \right| = 1 - \mathrm{CV}, \tag{8}$$

where $1/\Delta t$ is the sampling rate of the discrete time series and CV denotes the *circular variance* [26] of an angular distribution obtained by transforming the relative phase angles onto the unit circle in the complex plane. [1] Note that this measure may easily be adapted to the investigation of $n : m$ synchronization by replacing $\varphi_{1,1}$ by $\varphi_{n,m}$.

[1] In principle, the phase of $\frac{1}{N}\sum_{j=0}^{N-1}\mathrm{e}^{\mathrm{i}\varphi_{1,1}(j\Delta t)}$ is also a relevant observable but in this paper we restrict ourselves to the investigation of R.

The use of Euler's formula turns (8) into

$$\begin{aligned}R = \Bigg(&\left[\frac{1}{N} \sum_{j=0}^{N-1} \sin\left[\varphi_{1,1}(j\Delta t)\right] \right]^2 \\ &+ \left[\frac{1}{N} \sum_{j=0}^{N-1} \cos\left[\varphi_{1,1}(j\Delta t)\right] \right]^2 \Bigg)^{1/2}.\end{aligned} \tag{9}$$

From this notation it becomes evident that R, being restricted to the interval $[0, 1]$, reaches the value 1 if and only if the condition of strict phase *locking* is obeyed whereas for a uniform distribution of phases (which would be expected, on the average, for unsynchronized time series) results in $R = 0$.

To illustrate the difference between the (time-averaged) relative frequency and the mean phase coherence, Fig. 1 shows a comparison between the two measures for diffusively coupled Rössler systems (cf. [27]):

$$\begin{aligned}\dot{x}_{1,2} &= -\omega_{1,2}y_{1,2} - z_{1,2} + \varepsilon(x_{2,1} - x_{1,2}), \\ \dot{y}_{1,2} &= \omega_{1,2}x_{1,2} + 0.165y_{1,2}, \\ \dot{z}_{1,2} &= 0.2 + z_{1,2}(x_{1,2} - 10) \\ \text{with } \omega_1 &= 0.89 \text{ and } \omega_2 = 0.85,\end{aligned} \tag{10}$$

plotted versus the coupling strength ε both in the absence of noise and in the case of signals contaminated with additive uniform white noise at a signal to noise ratio (SNR) of 1. The graphs show that the mean phase coherence is far more robust for noisy time series. Note that R exhibits a similar course as the *similarity function* used in [27].

Due to this robustness against noise, the mean phase coherence can be regarded as a suitable measure for phase synchronization in biological time series such as the EEG.

3. Analysis of the EEG of epilepsy patients

The analyzed EEG signals were recorded from epilepsy patients undergoing presurgical diagnostics. The recording was performed under video control using chronically implanted intracranial depth electrodes (see Fig. 2 for a schematic view of

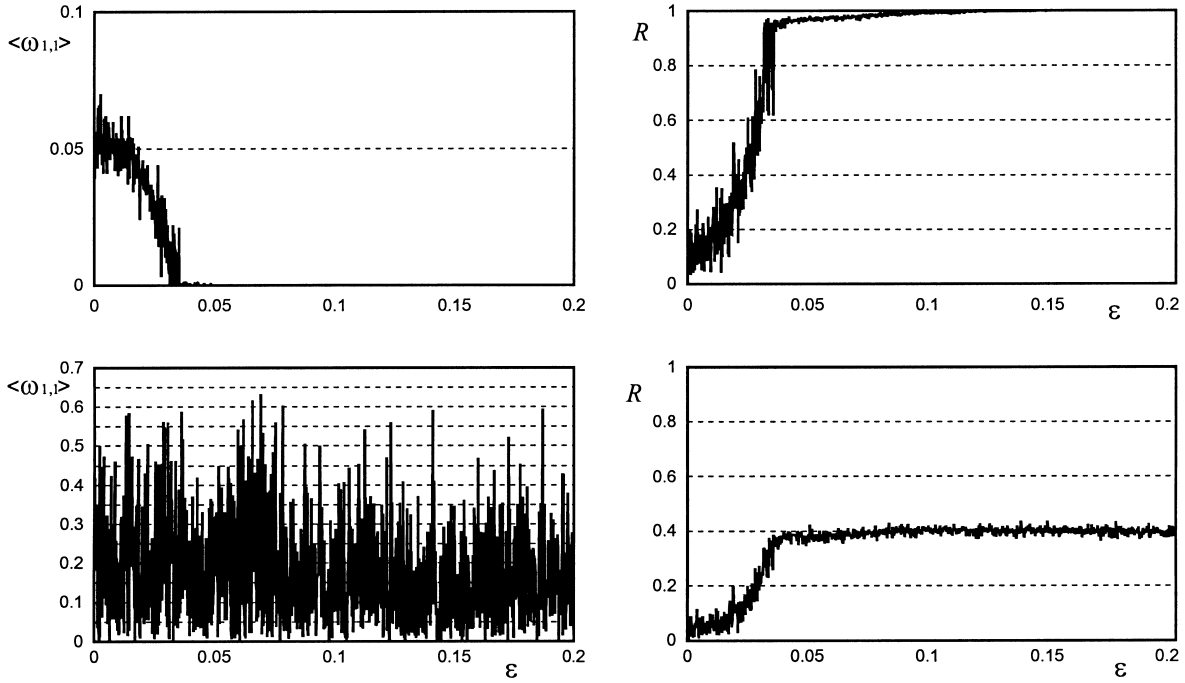

Fig. 1. Time-averaged relative frequency $\langle\omega_{1,1}\rangle$ and mean phase coherence R as a function of coupling strength ε for the x-coordinates of diffusely coupled Rössler systems. Upper plots: no noise contamination. Lower plots: signals contaminated with additive white noise at an SNR of 1.

implantation), each equipped with 10 contacts of a nickel–chromium-alloy (length: 2.5 mm, intercontact distance: 4 mm). After neurosurgical implantation, the correct placement of the electrodes was verified by magnetic resonance imaging.

The EEG recording was carried out on a 128-channel amplifier system using band-pass filter settings of 0.5–85 Hz (12 dB/oct.) using an average common reference. The sampling rate was 173.61 Hz and analog–digital-conversion was performed at 12 bit resolution. To give an impression of the analyzed data, Fig. 3 shows different EEG epochs from one patient along with the corresponding power spectra.

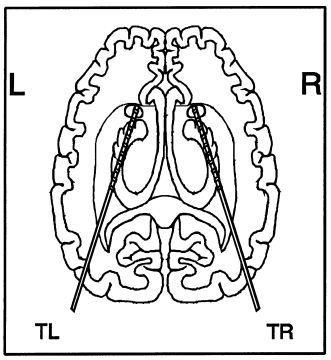

Fig. 2. Schematic view of intracranially implanted depth electrodes.

For our study 17 patients were selected all of whom have achieved complete post-operative seizure control after resection of what was correctly assumed to be the primary epileptogenic focus. This means that for all of these patients, the localization of the epileptogenic focus can be presumed to be known. In 11 patients the focus was localized on the left brain hemisphere, while in six patients the focus was on the right-hand side. In the following we refer to the brain hemisphere containing the epileptogenic focus as the *focal side*, whereas the opposite hemisphere is denoted as the *nonfocal side*.

The data were analyzed by using a moving-window-technique, which represents a common way of handling large amounts of data, especially for the

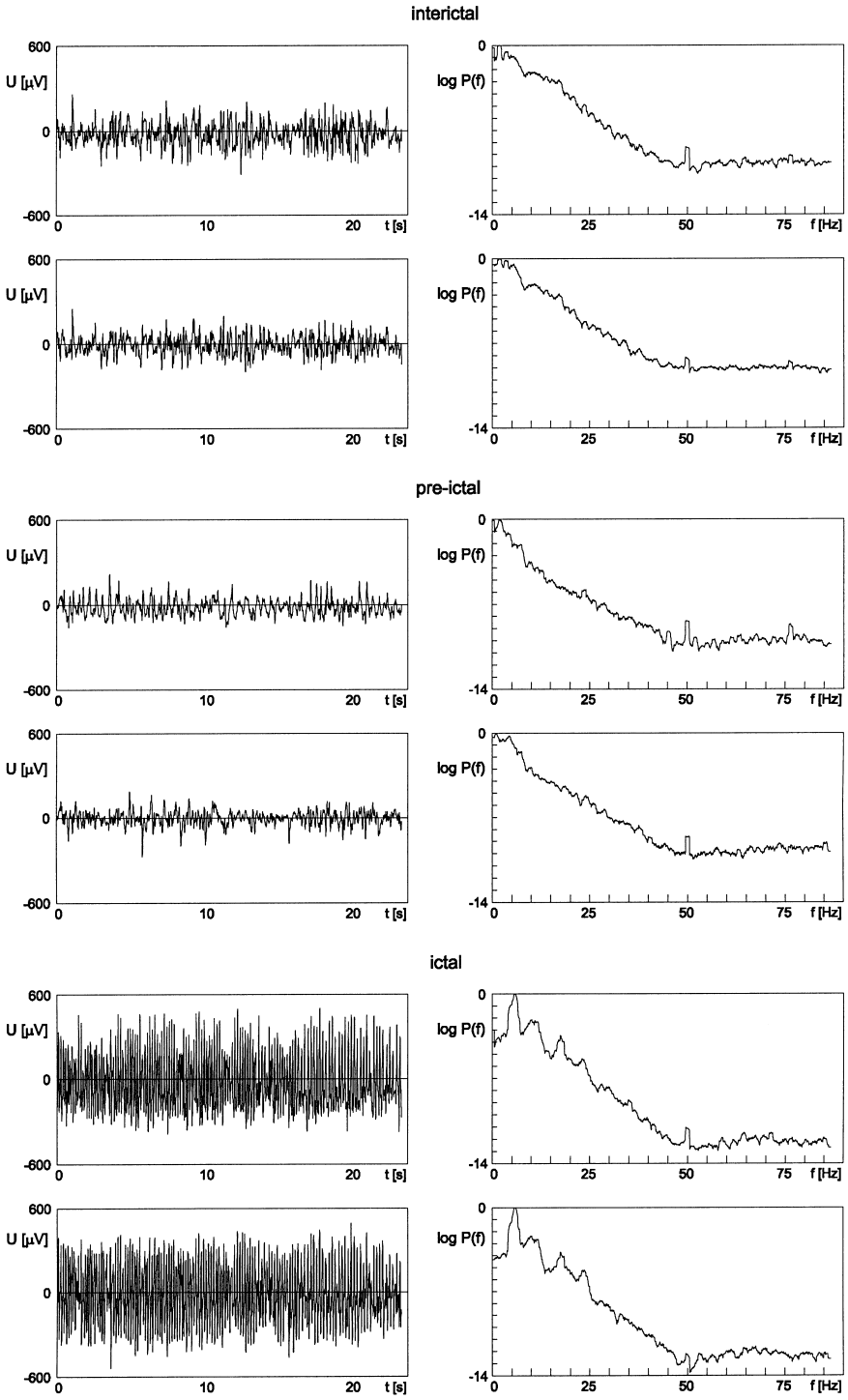

Fig. 3. Typical EEG segments (left) and corresponding normalized power spectra (right). Data were obtained from adjacent recording sites (cf. Fig. 2) during an interictal (no seizure activity), pre-ictal (minutes before an impending seizure), and ictal (during a seizure) state. Computation of the mean phase coherence R (cf. Eq. (8)) for these segments yielded 0.83, 0.37, and 0.94, respectively.

EEG [28]. The time series were divided into segments of 4096 sampling points each, corresponding to a window length of 23.6 s at the given sampling rate, and windows overlapped by 20%. This segment length can be regarded as a compromise between the required statistical accuracy for the calculation of the mean phase coherence and approximate stationarity of the data within a window's length [29]. Since the most time-consuming part of the algorithm is a fast Fourier transform (FFT) algorithm for calculation of the Hilbert transform (cf. Eq. (6)), the computational speed of the algorithm depends on the window length of N sampling points like $N \log N$.

Prior to the calculation of the mean phase coherence, three steps of data pre-processing were performed for each data window: first, the data of each window were demeaned which corresponds to setting the DC Fourier coefficient ($\omega = 0$) to zero. Next, to avoid edge effects, each window was tapered using a cosine half wave (Hanning window) before performing the Fourier transform. Finally, since the calculation of the Hilbert transform requires integration over infinite time, which cannot be performed for a window of finite length, 10% of the calculated instantaneous phase values are discarded on each side of every window.

4. Interpretation of results

4.1. Spatial variability of synchronization

Before investigating the spatial variability of the mean phase coherence as a measure of synchronization, it is important to realize that there is no straightforward way of projecting the *bivariate*, symmetric phase coherence calculated from signals measured at two different locations to a single point or region within the brain. The question whether the mean phase coherence should be projected onto one of the respective electrode contacts, onto both of them, onto their line of interconnection, or onto the middle of this line, respectively, remains a nontrivial problem to be discussed.

For our analysis, 40 artifact-free interictal EEG segments (mean duration: 34 min) recorded from the 17 patients were evaluated by applying the moving-window-technique as described above to every possible combination of electrode contacts for the left and right brain hemisphere, respectively. Since the mean phase coherence graphs showed little variance over time, a time-averaging over all windows of each EEG recording was performed, resulting in a matrix of averaged coherence values for each hemisphere.

An example of such a matrix is shown in Fig. 4. The values of the mean phase coherence have been coded using a gray-scale for better visualization. Each matrix features two regions of high synchronization (dark areas): In the left electrode, the contacts TL1–TL4 and TL5–TL10, respectively, show a high mutual phase coherence. In the right electrode, this effect can be observed for contacts TR1–TR3 and TR5–TR10, respectively. Evaluation of the post-implantational MRI scan of this patient revealed that the contacts corresponding to these regions of high phase coherence were in fact located within different anatomical structures of the brain: TL1–TL4 and TR1–TR3 were located within the entorhinal cortex, while TL5–TL10 and TR5–TR10 were located in the hippocampal body. Thus, analyzing the mean phase coherence of EEG channels recorded from different anatomical structures of the brain reveals a high intrinsic synchronization within these structures, while synchronization between these structures is significantly lower. These findings correspond well with histological evaluations [30] in which synaptic connections between neurons within these brain structures were found to be far more numerous than connections between these structures. Moreover functional analyses of memory formation showed the hippocampus and the entorhinal cortex to act as different modules within the same processing system [31]. Our results confirm to those of Arnhold et al. [32], where mutual interdependence was used as an estimate for synchronization.

Clinical evaluation of a seizure recording from the patient analyzed in Fig. 4 showed that seizure activity started in channels TL7–TL9, which show indeed a perceptibly higher level of interictal mutual synchronization than the corresponding channels on the nonfocal side. Evaluation of other patients led to similar results.

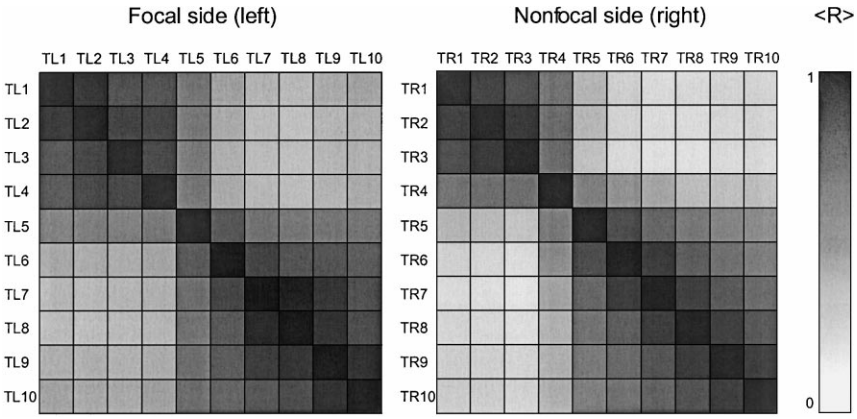

Fig. 4. Time-averaged phase coherence matrices extracted from an interictal recording (no seizure activity, patient No. 1 in Fig. 5). Each matrix reveals two areas of high synchronization (left-hand side: TL1–TL4 and TL5–TL10; right-hand side: TR1–TR3 and TR4–TR10). In ictal segments (seizure activity, not shown here), seizure activity for this patient was first discernible in TL7–TL9.

It must be emphasized that the mean phase coherence of brain-electrical time series is not at all homogeneous but on the contrary strongly depends on the exact location of the electrode contacts. This effect makes comparison of the focal and nonfocal phase coherence matrices quite difficult: suppose, for instance, that all contacts of the right electrode in Fig. 4 were positioned within the hippocampal formation, then the average level of the mean phase coherence would seem higher as compared to the focal side due to the fact that the matrix would consist entirely of high intrinsic synchronization values.

Regardless of these problems, we tried to get a first estimate of our measure's sensitivity to pathological synchronization by simply spatially averaging over the (already time-averaged) phase coherence matrices for every patient. The focal and nonfocal values of the resulting measure $\bar{R}$ for each patient are shown in Fig. 5. Multivariate analysis of variance (ANOVA) using F-statistics revealed significant influence of the

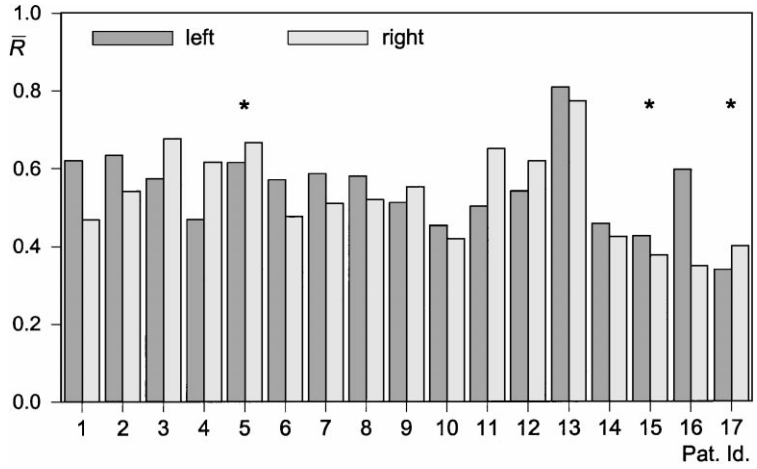

Fig. 5. Lateralization plots from interictal EEG recordings for 17 patients comparing left and right mean phase coherence averaged over space and time. Asterisk denotes false lateralization in the sense that the mean phase coherence is higher on the nonfocal side.

side of the epileptogenic focus on focal and nonfocal $\bar{R}$ values ($p = 0.017$). For the entire group of patients, the averaged mean phase coherence was indeed higher on the focal side (0.57 ± 0.11 vs. 0.50 ± 0.10; Wilcoxon signed rank test: $Z = -2.72$; $p = 0.006$). This effect allowed to correctly lateralize the side of the epileptogenic focus in 14 out of 17 patients. Considering the crudeness of this method, this can be regarded as a good result in the sense that the mean phase coherence indeed appears to be a measure that is sensitive to pathological synchronization associated with epilepsy even during seizure-free intervals.

4.2. Temporal variability of synchronization

An important issue in epileptology is whether specific features can be extracted from time series of brain electrical activity that are predictive of an impending seizure. Much research has been done on this topic lately, and different approaches have been used [33–37]. In order to find characteristic differences between interictal recordings (i.e. recordings containing no seizure activity) and pre-ictal recordings (i.e. recordings before a seizure), we evaluated the time course of each of the 45 different combinations of channels on the focal side for every recording and manually selected the combination that showed the most distinct differences between interictal and pre-ictal recordings. As an example, the results for two patients (patients No. 2 and 13 in Fig. 5) are given in Figs. 6 and 7, respectively. Evaluation of the respective data protocols revealed that during all of the recordings, the patients were under similar conditions (awake, at rest).

For the interictal recordings, the course of the mean phase coherence R is quite stable at a high, constant level in both patients. The peri-ictal recordings (before, during, and after a seizure), which started 15–35 min before the seizure, show a completely different picture: at the beginning of the recordings, R shows a significantly lower level as well as a higher variance in both patients. High peaks of R are observed during the seizures in both patients. For the first patient there is an increasing trend of coherence in the pre-ictal phase which is stopped by the onset of the seizure. The actual seizure is immediately followed by a drop in phase coherence, which after 3–4 min returns to a course similar to the interictal recordings. For the second patient, there is no distinct trend but the low level of phase coherence is interrupted by many narrow peaks. After the seizure, the mean phase coherence immediately returns to a course similar to the

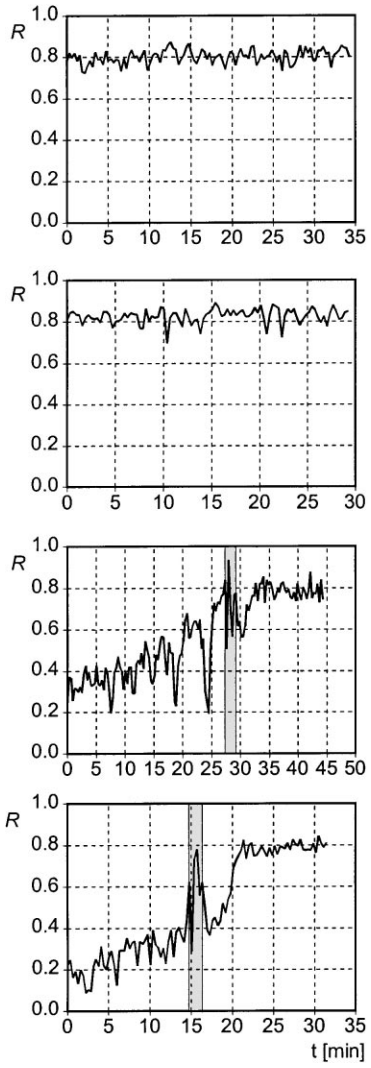

Fig. 6. Mean phase coherence calculated from interictal and peri-ictal EEG recordings (patient No. 2 in Fig. 5, channels TL1 and TL2) recorded on different days. Seizures are marked by vertical gray bars. Coherence values $R > 0.04$ can be assumed to be statistically significant at a level of $p = 0.01$ (Rayleigh test for uniformity, cf. [26]).

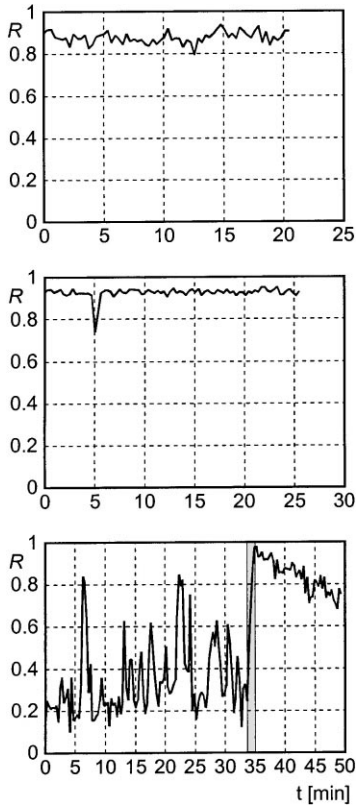

Fig. 7. Same as Fig. 6 but for patient No. 13 in Fig. 5 (channels TL7 and TL8).

interictal recordings. These surprising results will be discussed in more detail in the next section.

5. Discussion

The results indicate that phase synchronization between two EEG channels as measured by the mean phase coherence R appears to be related to pathological findings in epilepsy patients. Moreover, the ability of the measure to reflect anatomical boundaries of brain structures due to their high intrinsic synchronization renders it a possible tool for functional analysis of specific brain functions such as memory formation. However, it is this intrinsic synchronization in different anatomical structures that makes it difficult to separate physiological from pathological synchronization. Furthermore, the problem of using the bivariate mean phase coherence to characterize just one specific point or region within the brain along with the difficulty that the stereotactically implanted electrodes are often not positioned in perfect symmetry makes a direct comparison of the focal and nonfocal brain hemisphere rather difficult.

Nevertheless, even crude spatial averaging over the synchronization matrices during interictal periods revealed an excess synchronization on the side of the epileptogenic focus in more than 82% of the patients. This indicates that the epileptogenic focus indeed distinguishes itself by a pathologically increased level of synchronization, which is in accordance with the current theories on epileptogenesis.

The capability of determining the side or even the exact location of an epileptogenic focus without the necessity of registrating actual seizure activity would be of high diagnostical value. It must be noticed, however, that other measures from nonlinear time series analysis have been proposed which seem to be better suited for this purpose [33,38,39]. Since these measures are univariate, they can more easily be projected onto the brain's topography. Furthermore, a hemispherical average over a univariate measure is less affected by variations in electrode placement than that over a bivariate measure. On the other hand, an important advantage of a bivariate measure like R is the possibility of examining long distance effects such as affection of adjacent and remote brain areas, e.g. the synchronization between the hippocampus and cortical regions of the brain.

Another interesting result is the characteristic difference in mean phase coherence between interictal and peri-ictal EEG recordings as shown for two of the patients. Although any general conclusion drawn from such a limited number of patients must be regarded as rather speculative, several effects might explain the observed phenomena.

The low level of R at the beginning of the peri-ictal recordings suggests that there may have been a drop of the mean phase coherence some time ahead of these recordings. In this context, an epileptic seizure might be interpreted as the "tip of the iceberg" in the sense that it is just the climax of a process of changes in brain dynamics that starts long before the seizure.

Although there is only limited knowledge about seizure-generating mechanisms in humans, model simulations and animal experiments have led to the theory that seizure activity will be induced when a "critical mass" of neurons is progressively involved in synchronized high-frequency discharging ([35] and references therein). It is therefore surprising that the pre-ictal periods observed in this study are contrarily characterized by a decreased level of synchronization. One hypothesis to explain this phenomenon is that the decrease in synchronization found between the two electrode contacts is due to the fact that both contacts are located within different areas of synchronization. If for instance one contact was located within neuronal tissue already involved in the pathological synchronization progressing from the epileptogenic focus while the other was located in a region still belonging to some process of physiological synchronization, then the level of synchronization between these contacts would be expected to be low. Another hypothesis is that neurons not involved in any synchronized physiological process may more easily be recruited into a critical mass. Thus, the state of decreased pre-ictal synchronization tracked by the mean phase coherence could be regarded as a state of increased susceptibility for pathological synchronization, thereby possibly representing a lowered threshold for seizure activity (cf. [32]).

Moreover, it is remarkable that shortly after a seizure, the mean phase coherence returns to a level similar to that found in the interictal recordings. This observation corresponds to the hypothesis that an epileptic seizure can act as some type of a resetting mechanism from an unstable to a more stable state of brain dynamics [40]. A question to be subjected to further research is whether an epileptic seizure is the only mechanism by which the brain returns from a pathological state of decreased synchronization to one of interictal (physiological) synchronization (specificity of the observed effect) and whether an epileptic seizure is necessarily preceded by a state of altered synchronization (sensitivity of the observed effect). Provided that the analyzed recordings are in fact representative of these patients' epileptic activity (i.e. that any other interictal or peri-ictal recordings exhibit similar characteristic features), the distinct differences in level and variation would offer the possibility of distinguishing a pre-ictal from an interictal state, thus rendering helpful information for an actual prediction of seizures. It must be taken into account, however, that the difference in variability could also be caused by the effect that interictal levels of mean phase coherence are close to 1 (the upper limit), so changes in synchronization can no longer be resolved as distinct.

In comparison to other measures from nonlinear time series analysis used for the purpose of seizure prediction [35–37], which seem to be capable of detecting characteristic changes in the EEG minutes in advance of the seizure, it appears that the observed changes in mean phase coherence occur on a larger time scale, possibly hours before an actual seizure. This indicates that the changes in brain dynamics which can be traced by the mean phase coherence may be different from those traced by other measures, possibly making the mean phase coherence a valuable addition to these measures.

6. Conclusions

In the present study, we have applied the concept of phase synchronization to time series of brain electrical activity recorded from epilepsy patients to investigate whether spatial or temporal changes in synchronization can be related to pathological activity. We have followed the approach of understanding phase synchronization in a statistical sense [13] and applied a straightforward measure for phase synchronization employing the circular variance of a phase distribution. After testing the robustness of this measure for noisy time series, we used it to measure the phase synchronization of EEG recordings.

Our results indicate a sensitivity of this measure for both physiological and pathological synchronization of neuronal activity. In agreement with current theories on epileptogenesis, we found evidence that the epileptogenic focus is characterized by an increase in synchronization as measured by the mean phase coherence even in time intervals far away from any actual seizure activity. Furthermore, evidence was found

that epileptic seizures can be preceded by characteristic changes in synchronization. From this we conclude that further analyses of phase synchronization changes in EEG recordings from epilepsy patients might help to gather more insight into the epileptogenic process. Further investigations are currently carried out.

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