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Information-theoretical analysis of resting state EEG microstate sequences - non-Markovianity, non-stationarity and periodicities

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ABSTRACT

We present an information-theoretical analysis of temporal dependencies in EEG microstate sequences during wakeful rest. We interpret microstate sequences as discrete stochastic processes where each state corresponds to a representative scalp potential topography. Testing low-order Markovianity of these discrete sequences directly, we find that none of the recordings fulfils the Markov property of order 0, 1 or 2. Further analyses show that the microstate transition matrix is non-stationary over time in 80% (window size 10 s), 60% (window size 20 s) and 44% (window size 40 s) of the subjects, and that transition matrices are asymmetric in 14/20 (70%) subjects. To assess temporal dependencies globally, the time-lagged mutual information function (autoinformation function) of each sequence is compared to the first-order Markov model defined by the classical transition matrix approach. The autoinformation function for the Markovian case is derived analytically and numerically. For experimental data, we find non-Markovian behaviour in the range of the main EEG frequency bands where distinct periodicities related to the subject's EEG frequency spectrum appear. In particular, the microstate clustering algorithm induces frequency doubling with respect to the EEG power spectral density while the tail of the autoinformation function asymptotically reaches the first-order Markov confidence interval for time lags above 1000 ms. In summary, our results show that resting state microstate sequences are non-Markovian processes which inherit periodicities from the underlying EEG dynamics. Our results interpolate between two diverging models of microstate dynamics, memoryless Markov models on one side, and long-range correlated models on the other: microstate sequences display more complex temporal dependencies than captured by the transition matrix approach in the range of the main EEG frequency bands, but show finite memory content in the long run.

1. Introduction

The most prominent features of resting state surface EEG recordings are ongoing, amplitude-modulated oscillations across the frequency range of approximately 0.5− 70 Hz (Niedermeyer and da Silva, 2005). EEG data is often analyzed with respect to this oscillatory activity. For instance, we may be interested in the spectral power of a given frequency band, phase relationships, or the dynamics of the oscillation's envelope, to name but a few. The spatial distribution of the scalp potential varies over time, showing episodes of stability alternating with short transition episodes between certain quasi-stable EEG topographies (Wackermann et al., 1993). Applying data compression techniques, stable topographies can be clustered into sets of a few maps maximizing the global explained variance (GEV) (Wackermann et al., 1993; Murray et al., 2008). These maps are fitted competitively into the original EEG time series using a maximum correlation criterion at each time step. The resulting microstate sequence at each time step contains the microstate label whose map has the maximum absolute correlation with the EEG topography at that time point. Alternative implementations have been proposed (Koenig et al., 1999). Microstates denote quasi-stable episodes corresponding to a single representative map, with an average duration in the range of 10–100 ms (Koenig et al., 2002; Brodbeck et al., 2012). Many studies have shown a set of $n = 4$ microstates to be optimal (Murray et al., 2008; Brodbeck et al., 2012) although other cluster numbers have been described in healthy resting state (Yuan et al., 2012) and pathological conditions (Koenig et al., 1999; Kuhn et al., 2015). Here, we mostly use $n = 4$ microstates, however, all methods presented here can be used for any number of states.

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The most common approach to microstate analysis is the transition matrix approach. Using this straightforward approach, the transition probabilities between microstate maps are estimated from the empirical sequence of map labels and the resulting matrix is normalized row-wise in order to yield a stochastic matrix. Subsequently, different experimental conditions can be related to changing matrix entries (Koenig et al., 2002; Brodbeck et al., 2012; Kuhn et al., 2015). On a conceptual level, the transition matrix approach implies a (first-order) Markovian model as the information flow over time is summarized by the conditional probability of the future state $x_{t+1} = S_j$, given the current state $x_t = S_i$. Therefore, temporal dependencies more complex than first-order Markov models cannot be captured by this approach. Moreover, calculating a fixed transition matrix for a given data set cannot model transition dynamics changing over time, i.e. non-stationarities. Unfortunately, the Markov property is almost never tested for, an exception being the microstate duration analysis published by (Wackermann et al., 1993). Testing the geometric distribution of microstate durations for short EEG time series up to a duration of 16 s, the Markov property could not be rejected in 22/24 data sets (Wackermann et al., 1993). For longer time series of at least several minutes, as usually recorded in resting state experiments, we are not aware of any formal tests of low-order Markov properties.

As an alternative analysis tool, Hurst exponent estimation has recently been introduced for microstate sequences, with the aim to find possible long-range dependencies (LRD) (Van de Ville et al., 2010; Gschwind et al., 2015). In order to estimate the Hurst exponent, the n-state symbolic sequence has to be mapped to a metric space $\{-1, +1\}$ using a partition of the state space (Van de Ville et al., 2010). The technique is inspired by LRD analyses of 4-state DNA sequences (Peng et al., 1992). However, the following two questions remain unanswered so far: a) which is the correct state space partition, i.e. which EEG topographies should be lumped into one group, and b) how can the technique be applied to arbitrary cluster numbers? Moreover, the resulting Hurst exponents are difficult to interpret as a Hurst exponent of $H > 0.5$ does not automatically imply long-range dependencies, especially in the case of non-stationary signals (McCauley et al., 2007; Riley et al., 2012). We recently reported an excessive proportion of false-positive LRD results when comparing experimental data with short-range correlated Markov models (von Wegner et al., 2016).

The aim of the current study is to systematically analyze temporal dependencies of microstate sequences and to characterize these sequences in the language of stochastic processes. Without making assumptions on symbol distributions and their temporal dependencies, we compute estimates of various information-theoretical quantities. Using this approach, we avoid the need to partition the microstate set and to project the sequences onto a metric space. All quantities used can be computed for arbitrary state spaces, i.e. for any number of microstates.

Our analysis starts on the shortest time scales, assessing low-order Markov properties (order 0– 2) directly, based on well-established statistical tests (Kullback, 1959; Kullback et al., 1962). We perform an additional first-order Markovianity test using a method presented in the context of microstate research (Wackermann et al., 1993). Next, the transition matrix is tested for time-stationarity, also termed conditional homogeneity in (Kullback, 1959; Kullback et al., 1962), and for symmetry. Finally, global temporal dependencies up to time lags of 2000 ms are analyzed using the time-lagged mutual information function (auto-information function). Distinct periodicities found there are further tested for robustness with respect to individual microstate maps and to cluster numbers.

The information-theoretical approach presented here lets us conclude that microstate properties show a behaviour somewhere between memoryless Markov models and possibly long-range correlated random walk models, adding the unique feature of reflecting the underlying EEG periodicities.

2. Material & methods

2.1. Experimental data

A set of EEG recordings from 20 right-handed healthy subjects during wakeful rest (age range: 19– 27, mean age: 23 yrs) was recorded in an eyes-closed, wakeful rest condition. Selection criteria for the recordings used were steady, prominent alpha oscillations in the parieto-occipital EEG channels, and the absence of artefacts (eye blink, muscle, electrode artefacts) or signs of drowsiness. The 30 channel EEG data sets were acquired at a sampling rate of 5 kHz using the standard 10– 10 electrode configuration. Data were band-pass filtered to 1– 40 Hz, down-sampled to 250 Hz and re-referenced to an average reference. Power spectral densities were computed with Welch's method using a segment length of 1024 samples, 50% overlap and a Hanning window. EEG recordings have a total duration ranging from 100 to 312 s, corresponding to lengths of 25000-78000 samples. Written informed consent was obtained from all subjects, and the study was approved by the ethics committee of the Goethe University, Frankfurt, Germany.

2.2. Microstate analysis

EEG microstates were computed using the modified K-means algorithm described in (Murray et al., 2008) and illustrated in Fig. 1. Fig. 1 shows a segment of resting-state EEG for a selection of channels as indicated to the left. In the first step, the global field power time series (GFP, blue line) is computed as the spatial standard deviation of the EEG topography at each given time. At local GFP maxima (red dots), the spatial configuration of the EEG is considered stable and explains most of the variance of the time series (Wackermann et al., 1993). Therefore, K-means clusters are initialized with EEG patterns drawn randomly from

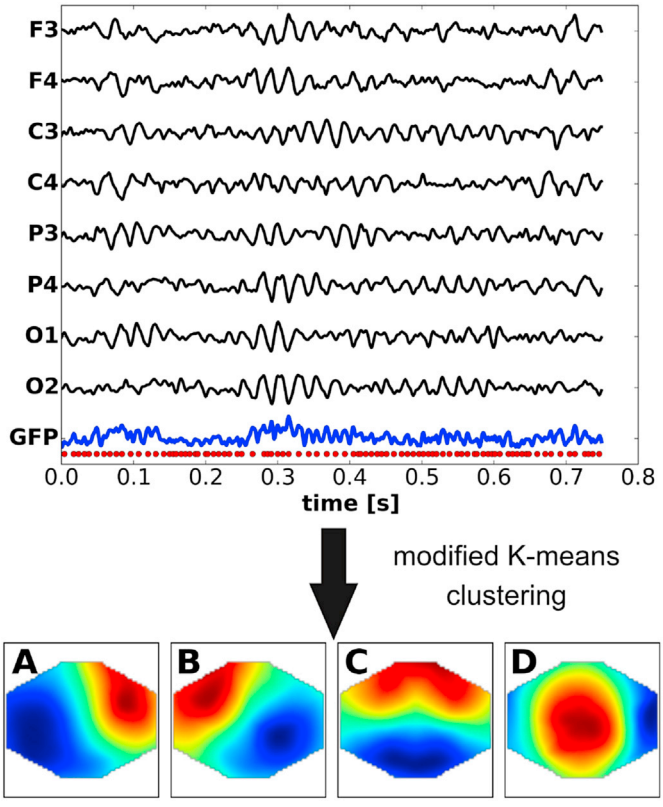

Fig. 1. Microstate segmentation: the top panel shows a section of resting state EEG (1–40 Hz, black lines) along with the resulting global field power (GFP, blue) and the local GFP maxima (red dots). For better visibility, only the EEG channels indicated to the left are shown. EEG topographies at local GFP maxima are clustered by the modified K-means algorithm to obtain the (n = 4) microstate maps labelled A-D (bottom panel).