Video Article

Microstate and Omega Complexity Analyses of the Resting-state Electroencephalography

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Abstract

Microstate and omega complexity are two reference-free electroencephalography (EEG) measures that can represent the temporal and spatial complexities of EEG data and have been widely used to investigate the neural mechanisms in some brain disorders. The goal of this article is to describe the protocol underlying EEG microstate and omega complexity analyses step by step. The main advantage of these two measures is that they could eliminate the reference-dependent problem inherent to traditional spectrum analysis. In addition, microstate analysis makes good use of high time resolution of resting-state EEG, and the four obtained microstate classes could match the corresponding resting-state networks respectively. The omega complexity characterizes the spatial complexity of the whole brain or specific brain regions, which has obvious advantage compared with traditional complexity measures focusing on the signal complexity in a single channel. These two EEG measures could complement each other to investigate the brain complexity from the temporal and spatial domain respectively.

Video Link

The video component of this article can be found at https://www.jove.com/video/56452/

Introduction

Electroencephalography (EEG) has been widely used to record electrical activity of the human brain both in clinical diagnosis and scientific research, since it is noninvasive, low-costed and has very high temporal resolution[1]. In order to study the EEG signals in resting state, researchers have developed many EEG techniques (e.g., power spectrum analysis, functional connectivity analysis)[2,3]. Of these, microstate analysis and omega complexity analysis could make good use of the spatial and temporal information inherent in EEG signals[4].

Previous researches have shown that although the topographical distribution of EEG signals varies over time in eye-closed or eye-open resting state, the series of momentary maps show discontinuous changes of landscapes, i.e., periods of stability alternating with short transition periods between certain quasi-stable EEG topographies[5]. Microstates are defined as these episodes with quasi-stable EEG topographies, which last between 80 and 120 ms[1]. Since different electric potential landscapes must have been generated by different neural sources, these microstates may qualify as the basic blocks of mentation and can be considered as "atoms of thought and emotion"[6]. Using modern pattern classification algorithms, four resting EEG microstate classes have been consistently observed, which were labeled as class A, class B, class C and class D[7]. Moreover, researchers revealed that these four microstate classes of resting EEG data were closely associated with well-known functional systems observed in many resting-state fMRI (functional magnetic resonance imaging) studies[8,9].Thus, the microstate analysis provided a novel approach to study the resting state networks (RSNs) of human brain. In addition, the average duration and the frequency of occurrence of each microstate class, the topographical shape of the four microstate maps are significantly influenced by some brain disorders[4,10,11], and are associated with fluid intelligence[12] and personality[13].

In the other aspect, traditional functional connectivity of multi-channel EEG could only describe the functional connections between two scalp electrodes, thus failed to assess the global functional connectivity across scalp or within a certain brain region. The omega complexity, proposed by Wackermann (1996)[14] and calculated through an approach combining principal component analysis (PCA) and Shannon entropy, has been used to quantify the broad-band global synchronization between spatially distributed brain regions. In order to assess the omega complexity of each frequency band, Fourier transform was commonly conducted as an initial step[25].

The microstates and omega complexity can be used to reflect two closely linked concepts, *i.e.*, the temporal complexity and spatial complexity[4]. Since the microstate classes represent certain mental operations in human brain, they can reflect the temporal structure of neuronal oscillations. Lower duration and higher occurrence rate per second must indicate higher temporal complexity. The omega complexity is positively related with the number of independent neural sources in brain, thus are commonly considered as an indicator of spatial complexity[4].

The current article describes the protocol of EEG microstate analysis and omega complexity analysis in detail. The EEG microstate and omega complexity analyses offer the opportunity to measure the temporal and spatial complexities of brain activity respectively.

Protocol

This protocol was approved by the local ethical committee. All the participants and their parents signed an informed consent form for this experiment.

1. Subjects

1. Only include 15 healthy male adolescent subjects, whose age ranges from 14 to 22 years (mean ± standard deviation: 18.3 ± 2.8 years).
   NOTE: The current protocol to analyze the microstate and omega complexity has been developed for healthy subjects, but is not restricted to this group only.

2. EEG data recording

1. Ask subjects to sit on a comfortable chair in a silent, temperature-controlled room, where the EEG data was recorded. Collect the 20-channel EEG data using the ANT EEG system in this protocol.
2. Put the cap on the subjects' head.
   1. In this study, use a cap with medium size, since it was suitable for most adolescent or male subjects. For children, please measure the head circumference of each subject, and determine the cap with suitable size.
   2. Place the electrode Cz at approximately 50% of the distance between inion and nasion and 50% of the distance between the left and right inter-aural indentations. Place the reference electrodes on the left and right mastoid bone, respectively. Place the other scalp electrodes at the standard locations according to the international 10-20 system.
      NOTE: An electrode system and EEG amplifier with 20 channels is sufficient for EEG microstate analysis and omega complexity analysis.
3. Fill all the electrodes with conductive gel by inserting a blunt needle through the electrodes. Use the conductive gel to lower the impedance. Keep all electrode impedances lower than 10 kiloohms (kΩ).
   1. During this period, provide some entertainment for the subjects (e.g., show a short film). If a dry electrode or a saline electrode is used, skip the step of injecting conductive gel.
4. Instruct the subjects to relax with eyes closed during the recording, which lasts 5 min. Use the digitization software to digitize and record the EEG signal. Use a sampling rate of at least 250 samples/s. Use an online filter broader than 0.1 and 80 Hz.
   NOTE: Although most commercial available electrode-amplifier systems use an active electrode system, which could improve the signal to noise ratio of EEG signal, do not place this system close to any electrical devices during EEG recording.

3. EEG Data Preprocessing

NOTE: EEG data could be preprocessed using various open source or commercial software. The instructions provided below are specific for EEGLAB. This is only one out of many available options to preprocess EEG data.

1. Import the raw EEG data to the EEG software (e.g., EEGLAB) (File | Import data | Using EEGLAB functions and plugins).
   NOTE: The raw EEG data recorded from various electrode-amplifier systems could be recognized by EEGLAB, such as EGI, ANT, Brain Vision recorder, and Neuroscan.
2. Load the channel location file into the EEG software (Edit | Channel locations). Although the EEG data and the channel names have been imported to EEGLAB, import a channel location file into the EEG software in order to obtain the spatial locations of these electrodes.
3. Remove the reference electrodes (Edit | Select data| Select data in channel range). In the option of "Select data in channel range" of the pop-up dialogue box, select only the recording electrodes and do not select the reference electrodes so that the reference electrodes can be removed. The data recorded in reference electrodes is not 'true' brain signal, since these two electrodes are placed on the left and right mastoid bone respectively.
4. Band pass filter the EEG data between 0.5 and 80 Hz (Tools | Filter the data | Basic FIR filter [new, default]). In the pop-up dialogue box, choose 5 for the "Lower edge of the frequency pass band (Hz)", and choose 80 for the "Higher edge of the frequency pass band (Hz)". Then click the button of "Ok".
5. Remove the power line noise with a notch filter between 49 and 51 Hz (Tools | Filter the data | Basic FIR filter [new, default]). In the pop-up dialogue box, choose 49 for the "Lower edge of the frequency pass band (Hz)", and choose 51 for the "Higher edge of the frequency pass band (Hz)", and select the option of "Notch filter the data instead of pass band". Then click the button of "Ok".
6. Correct the data portions contaminated by eye movements, electromyography (EMG) or any other non-physiological artifacts using the Blind Source Separation (BSS) algorithm[15]. For eye movements, click on Tools | Artifact removal using AAR 1.3 | EOG removal | Using BSS; for EMG, Tools | Artifact removal using AAR 1.3 | EMG removal using BSS.
7. Segment the pre-processed continuous EEG data into epochs, with epoch length of 2 s. To do this, write '*EEG = eeg_regepochs(EEG, 'recurrence', 2, 'limits',[0 2],'rmbase' ,NaN); pop_saveset(EEG)*', then hit the Enter key of the keyboard. A window will pop up that allows the saving of the segmented EEG data.
8. Import the segmented EEG data to the EEG software (File | Load existing dataset).
9. Reject EEG epochs with amplitude values exceeding ± 80 μV at any electrode (Tools | Reject data epochs | Reject data [all methods]).
10. Save the preprocessed EEG data (File | Save current dataset as).

4. EEG Microstate Analysis

NOTE: A modified version of the classical K-means clustering algorithm is used for microstate class analysis[16], which contains a bottom-up procedure and an up-bottom procedure. In the bottom-up procedure, the group-level microstate classes are identified using the spatial correlation as a clustering criterion. Then in the up-bottom procedure, each topographical map of each subject in each group is assigned to the EEG microstate class with maximum spatial correlation. For resting-state EEG microstate analysis, the polarity of topographical maps is commonly disregarded. EEG microstate class analysis could be done using various open source softwares, such as CARTOOL, sLORETA, EMMA and MapWin. The instructions provided below are specific for the EEGLAB plugin for Microstates. This EEGLAB plugin could be downloaded from https://sccn.ucsd.edu/wiki/EEGLAB_Extensions_and_plug-ins.

1. For each subject, load the preprocessed EEG data (File | Load existing dataset), convert reference channels to common average reference (Tools | Re-reference), and band pass filter the EEG data between 2 and 20 Hz (Tools | Filter the data | Basic FIR filter [new, default]).
2. Identify the four microstate maps in each subject (Tools | Microstates | identify microstate maps). In the pop-up dialogue box, choose 3 for the "Min number of classes", choose 6 for the "Max number of classes", choose 50 for the "number of restarts", choose "Max number of maps to use", and select the options of "GFP peak only" and "No polarity". Then click the button of "Ok".
3. Save the EEG data of each subject after identifying its own microstate maps (File | Save current dataset as).
4. Import the EEG datasets of all the subjects saved in the last step at once (File | Load existing dataset).
5. Identify the group-level microstate maps (Tools | Microstates | Average microstate maps across datasets). In the pop-up dialogue box, select the datasets of all subjects in the option "Choose sets for averaging". In the option "Name of mean", give a name for the group-level microstate maps. The default name is "GrandMean". Then click the button of "Ok". This will create a new data set named as "GrandMean", which stores the group-level microstate maps.
6. Manually sort the order of four group-level microstate maps according to their classic order (Plot | Edit microstate maps). In the pop-up, select "More", and then the number of maps shown becomes four. Select "Man. sort". In the pop-up dialogue box, enter the new order of four group-level microstate maps. Then click "Close".
7. Sort the order of the four microstate maps of each subject (Tools | Microstates | Sort individual microstate maps according to mean).
8. Save the microstate parameters of each subject (Tools | Microstates | Quantify microstates in dataset [mean template maps]), which will invoke two pop-up dialogue boxes sequentially.
    1. In the first dialogue box, select the data sets of all subjects. In the second dialogue box, select "4 Classes" for option "Number of Classes", select the options of "Fitting only on GFP peaks" and "Remove potentially truncated microstates", choose 30 for the "Label smoothing window (ms)" and choose 1 for the "Non smoothness penalty". Then click "Ok". A csv file which stores the microstate parameters will be saved on the computer.

5. Omega Complexity Analysis

1. Save the EEG data of each epoch and each subject in ASCII or txt format using customized script.An example of the customized script for step 5.1 could be found in the Supplementary Materials.
   NOTE: If the global omega complexity is computed, the EEG data of all the scalp electrodes are needed to export in ASCII or txt format. If the regional omega complexity is computed, export only the EEG data of electrodes in that scalp region. For example, in order to compute anterior omega complexity, export only the EEG data of electrodes in anterior region (i.e., Fp1, Fp2, F7, F3, Fz, F4 and F8); in order to compute posterior omega complexity, export only the EEG data of electrodes in posterior region (i.e., T5, T6, P3, P4, Pz, O1 and O2).
2. Compute the omega complexity of all discrete frequencies using the sLORETA software[17] (Utilities | Global connectivity). This software is available at http://www.uzh.ch/keyinst/loreta.htm.
3. Compute the omega complexity of each frequency band using customized script[26]. In our case, compute the omega complexity of the following eight frequency bands as the mean value within each frequency limit, which are delta (0.5-3.5 Hz), theta (4-7.5 Hz), alpha1 (8-10 Hz), alpha2 (10.5-13.5 Hz), beta1 (14-18 Hz), beta2 (18.5-30 Hz), gamma1 (30.5-48 Hz), and gamma2 (52-80 Hz)[4]. An example of the customized script for step 5.3 could be found in the Supplementary Materials.

Representative Results

EEG microstate

Grand mean normalized microstate maps are displayed in **Figure 1**. The electric potential landscapes of these four microstate classes identified here are very similar to those found in previous studies[4].

The mean and standard deviation (SD) of microstate parameters of the healthy subjects were shown in **Table 1**. For microstate class A, the occurrence rate was 3.44 ± 1.29 times/s, and the duration was 72 ± 13 ms. For microstate class B, the occurrence rate was 3.54 ± 0.85 times/s, and the duration was 71 ± 18 ms. For microstate class C, the occurrence rate was 3.85 ± 0.63 times/s, and the duration was 69 ± 9 ms. For microstate class D, the occurrence rate was 3.41 ± 0.78 times/s, and the duration was 66 ± 11 ms.

Omega Complexity

The value (mean ± SD) of global omega complexity of each frequency band in the healthy subjects was presented in **Table 2**. For delta band, the global omega complexity was 6.39 ± 1.34. For theta band, the global omega complexity was 5.46 ± 0.85. For alpha-1 band, the global omega complexity was 3.47 ± 0.8. For alpha-2 band, the global omega complexity was 3.87 ± 0.70. For beta-1 band, the global omega complexity was 5.36 ± 0.84. For beta-2 band, the global omega complexity was 6.16 ± 0.83. For gamma-1 band, the global omega complexity was 6.95 ± 1.07. For gamma-2 band, the global omega complexity was 6.88 ± 1.39.

The value (mean ± SD) of anterior omega complexity of each frequency band in the healthy subjects was shown in **Table 2**. For delta band, the anterior omega complexity was 4.84 ± 1.7. For theta band, the anterior omega complexity was 4.23 ± 1.48. For alpha-1 band, the anterior omega complexity was 3.44 ± 1.09. For alpha-2 band, the anterior omega complexity was 3.87 ± 0.97. For beta-1 band, the anterior omega complexity was 3.74 ± 0.81. For beta-2 band, the anterior omega complexity was 2.94 ± 0.59. For gamma-1 band, the anterior omega complexity was 1.98 ± 0.24. For gamma-2 band, the anterior omega complexity was 3.02 ± 0.59.

The value (mean ± SD) of posterior omega complexity of each frequency band in the healthy subjects was shown in **Table 2**. For delta band, the posterior omega complexity was 3.71 ± 1.48. For theta band, the posterior omega complexity was 2.47 ± 0.85. For alpha-1 band, the posterior omega complexity was 2.11 ± 0.9. For alpha-2 band, the posterior omega complexity was 3.16 ± 1.42. For beta-1 band, the posterior omega complexity was 4.32 ± 1.67. For beta-2 band, the posterior omega complexity was 3.84 ± 1.04. For gamma-1 band, the posterior omega complexity was 2.17 ± 0.37. For gamma-2 band, the posterior omega complexity was 2.99 ± 0.53.

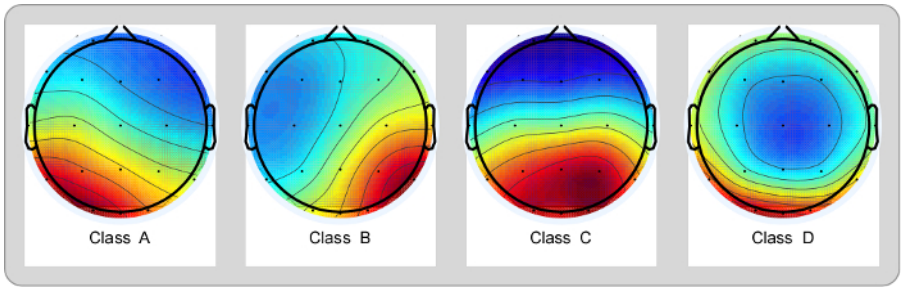

Figure 1. Mean normalized topographical maps of the four microstate classes (A-D) of resting-state EEG in the healthy subjects. Microstate class A and B have a right frontal to left occipital orientation and a left frontal to right occipital orientation, respectively. Microstate class C and D have symmetric topographies, but prefrontal to occipital orientation and frontocentral to occipital orientation were observed, respectively. Please click here to view a larger version of this figure.

	Microstate classes							
	A		B		C		D	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Occurrence/s	3.44	1.29	3.54	0.85	3.85	0.63	3.41	0.78
Duration (ms)	72	13	71	18	69	9	66	11

Table 1. Microstate parameters of the healthy subjects (n=15). The mean and standard deviation (SD) of the occurrence rate and duration of the four microstate classes were shown in this table.

	Global Omega Complexity		Anterior Omega Complexity		Posterior Omega Complexity	
Frequency Band	Mean	SD	Mean	SD	Mean	SD
Delta	6.39	1.34	4.84	1.7	3.71	1.48
Theta	5.46	0.85	4.23	1.48	2.47	0.85
Alpha-1	3.47	0.8	3.44	1.09	2.11	0.9
Alpha-2	3.87	0.7	3.87	0.97	3.16	1.42
Beta-1	5.36	0.84	3.74	0.81	4.32	1.67
Beta-2	6.16	0.83	2.94	0.59	3.84	1.04
Gamma-1	6.95	1.07	1.98	0.24	2.17	0.37
Gamma-2	6.88	1.39	3.02	0.59	2.99	0.53

Table 2. Global, anterior and posterior omega complexity of the healthy subjects (n=15). The mean and standard deviation (SD) of the global, anterior and posterior omega complexity for the eight frequency bands (delta, theta, alpha-1, alpha-2, beta-1, beta-2, gamma-1, gamma-2) were shown respectively in this table.

Supplemental Files. In order to run the scripts used in this manuscript, please open the scripts in the MATLAB environment, then copy all the content into the command window and press the "Enter" key. Note that, the scripts only apply to our data sets. Certain modifications are needed when the scripts are applied to other data sets. Please click here to download this file.

Discussion

In this article, two kinds of EEG analytic methods (i.e., microstate analysis and omega complexity analysis), measuring the temporal complexity and spatial complexity of human brain respectively, were described in detail. There are several critical steps within the protocol that should be mentioned. Firstly, the EEG data must be cleaned before the computation of the microstate and omega complexity. Secondly, the EEG data should be remontaged against the average reference before the computation of the microstate and omega complexity. Thirdly, the continuous EEG data must be segmented into epochs before the computation of the microstate and omega complexity. The length of each epoch should be

2 s. Lastly, the software that can be used in microstate analysis include Cartool (https://sites.google.com/site/cartoolcommunity/about), sLORETA (http://www.uzh.ch/keyinst/loreta.htm), and MapWin (http://www.thomaskoenig.ch/index.php/software/mapwin). The microstate analysis was conducted by means of one plugin in the EEGLAB in this study.

Although the microstate analysis conducted here was applied to resting state EEG data, it could be easily applied to event-related potentials (ERPs), which will help us uncover more information about the time courses of diverse cognitive operations in cognitive experiments, and provide a reference-free approach to perform ERP analysis[18,19]. Note, for resting state EEG, the polarity of topographical maps is commonly disregarded; however, for ERPs, the polarity of topographical maps should not be disregarded. A small limitation of this EEG plugin is that it could only be used for resting state EEG. For ERPs, the software Cartool may be one of the best choices. The omega complexity value attains from 1 to N. If omega complexity computed is 1, a maximum global functional connectivity within a certain brain region is revealed; whereas if omega complexity equals N, a minimum global functional connectivity within a certain brain region is found. Thus, if we want to statistically test the omega complexity of different brain regions, the number of electrodes selected in these regions must be equal, since the number of electrodes could significantly influence the value of omega complexity estimated.

In order to study the resting EEG, researchers have developed many EEG techniques (e.g., power spectrum analysis, functional connectivity analysis)[2,3]. Compared to these traditional techniques, microstate analysis takes full advantage of the excellent temporal resolution of EEG technique. The four identified microstate classes were found to be correlated with four well-studied functional systems observed in many resting-state fMRI studies[8,20]: auditory (microstate A), visual (microstate B), partially cognitive control and partially default mode (microstate C), and dorsal attention (microstate D). Thus, the microstate analysis provided a novel approach to study the resting state networks (RSNs) of human brain. Compared to traditional EEG techniques, the omega complexity could characterize the global functional connectivity within a certain brain region[4]. Traditional functional connectivity could only describe the functional connectivity between two scalp electrodes.

However, the two EEG techniques also have several limitations which should be mentioned. Firstly, the existing microstate analysis is commonly performed on broad-band EEG signals, thus it does not take advantage of the rich frequency information of the EEG technique. Moreover, the functional significance of these four microstate classes and related metrics are not very clear so far. Secondly, the omega complexity can only detect linear dependences. It cannot detect the nonlinear dependences between scalp regions, which could be quantified by some traditional functional connectivity metrics (e.g., phase-locking value, mutual information and synchronization likelihood)[21,22,23].

In the future, the microstate analysis should be applied with source localization techniques (e.g., sLORETA, BESA, Beamforming), which will significantly enhance the spatial resolution of EEG signals. Although the microstate analysis has been widely used in resting EEG and ERPs, only a few studies have applied this technique to the time-frequency domain. For example, Jia *et al.*[24] proposed an approach based on topographic segmentation analysis to optimally and automatically identify detailed time-frequency features. This approach could effectively exploit the spatial information of oscillatory activities. However, these applications are far from mature. For omega complexity, a normalized omega complexity is highly needed, since the value of omega complexity estimated is dependent on the number of electrodes selected. In the future, it should be applied to the time-frequency domain.

Disclosures

The authors have nothing to disclose.

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