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ORIGINAL PAPER

Classes of Multichannel EEG Microstates in Light and Deep Hypnotic Conditions

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Abstract The study assessed the brain electric mechanisms of light and deep hypnotic conditions in the framework of EEG temporal microstates. Multichannel EEG of healthy volunteers during initial resting, light hypnosis, deep hypnosis, and eventual recovery was analyzed into temporal EEG microstates of four classes. Microstates are defined by the spatial configuration of their potential distribution maps ('potential landscapes') on the head surface. Because different potential landscapes must have been generated by different active neural assemblies, it is reasonable to assume that they also incorporate different brain functions. The observed four microstate classes were very similar to the four standard microstate classes A, B, C, D [Koenig, T. et al. Neuroimage, 2002;16: 41–8] and were labeled correspondingly. We expected a progression of microstate characteristics from initial resting to light to deep hypnosis. But, all three microstate parameters (duration, occurrence/second and %time coverage) yielded values for initial resting and final recovery that were between those of the two hypnotic conditions of light and deep hypnosis. Microstates of the classes B and D showed decreased duration, occurrence/second and %time coverage in deep hypnosis compared to light hypnosis; this was contrary to microstates of classes A and C which showed increased values of all three parameters. Reviewing the available information about microstates in other conditions, the changes from resting to light hypnosis in certain respects are reminiscent of changes to meditation states, and changes to deep hypnosis of those in schizophrenic states.

Keywords EEG Microstates · Hypnosis · Multichannel EEG · Schizophrenia · Meditation

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Introduction

Among the various altered states of consciousness [1, 2], hypnosis is particularly interesting since it is installed by a hypnotist's mere verbal instructions to a consenting and able person, and since such instructions can result in important changes in information processing, for example in perception of experimentally induced pain [3, 4], in automatic visual processing [5] and in learning [6]. Hypnosis also is of practical interest because successful treatment of various conditions such as nausea, pain, anxiety, stress and depression can be achieved [7–12].

There is an extended literature on the physiology of brain functional mechanisms that underlie hypnosis (see e.g. [4, 5, 13–17]). The search for EEG characteristics that are specific for hypnosis was the topic of many studies, and after an initial predominance of spectral EEG analysis, many other analytical approaches were applied (e.g. [3, 18–25]). The typically hypothesis-driven designs and analyses often narrowed the results to fractions of the possible range so that comparisons between studies are limited. Hypnosis also poses a problem in experimental design since there is no straightforward control condition as there is no sham hypnosis. Further, since specific hypnotic suggestions are used to lead subjects into the different, specific hypnotic conditions, it is not surprising that these suggestions will be reflected by a variety of corresponding, specific brain electric activities. The few fMRI and PET studies on hypnosis also implicated activity of very different brain areas, and as in the case of EEG, some of these differences might parsimoniously be explained by the different hypnotic suggestions that were applied: e.g. predominant left anterior activity during pain reduction (fMRI: [26], PET: [3]), widespread left activity during pleasant memories (PET: [27], parietal-cerebellar activity during misattributions of self-movement to external sources (PET: [28], and occipital activity during relaxation (PET: [3]).

Our work group focuses on brain electric studies for the exploration of brain mechanisms of cognitive-emotional information processing. This approach offers a time resolution in the millisecond range as it is desirable for the investigation of perception and cognition. Analyzing multichannel EEG data as sequences of maps of the momentary spatial distributions of electric potential on the head surface, it became evident that brain activity over time consists of brief temporal epochs defined by a quasi-stable spatial distribution (‘potential landscape’) of brain electric activity; these epochs were called ‘microstates,’ and different microstates were found to incorporate different brain functions [29–32]. The duration of microstates is in the range of about 75–120 ms in spontaneous EEG. Our microstate results indicate that the seemingly continual stream of brain information processing, the subjective ‘stream of consciousness’ [33, 34] actually consists of subsecond building blocks of mentation, of ‘atoms of thought’ [31, 35]. Properties of certain classes of microstates vary with state of consciousness. Schizophrenic patients before medication differed from normal controls in that patients exhibited shortened duration of certain classes of microstates [36, 37]. On the other hand, microstate duration in one of the microstate classes was increased during advanced meditation [38].

The present study assessed brain electric organization measured as EEG microstates in healthy volunteers during initial resting, light hypnosis and deep hypnosis, and eventual post-hypnotic recovery resting. We expected a unidirectional progression of microstate characteristics from initial resting before hypnosis (and eventual resting in recovery) to light hypnosis to deep hypnosis, in other words, a continuum of EEG changes with deepening of hypnosis. This expectation was not born out: values for initial resting (or recovery) were between those for light hypnosis and deep hypnosis.

Materials and methods

Participants

Initially, 12 volunteers who were interested in hypnosis were recruited among Kansai Medical University hospital staff and medical students, with the following exclusion criteria: no history of drug abuse, head trauma, epileptic seizure, psychiatric disorders or other disease that might affect brain functions. The experimental design was accepted by the hospital’s ethics authorities; the design was explained to the participants who signed a written consent.

Of the 12 participants, eight reached the deep hypnotic condition as observed during and confirmed after the experiment, experiencing successfully the suggested amnesia for their own name and date of birth. One of these participants had to be excluded because of technical problems with the EEG data. Thus, the data of seven participants who had reached deep hypnosis remained for analysis (two males, five females; mean age 27.4 ± 9.7 years). They were all right-handed according to their self-reports.

Data recording

A psychotherapist with extensive experience as a hypnotist (K.S.) carried out the semi-structured hypnotic induction and the suggestions. The participant and the hypnotist were seated comfortably in the recording room, the hypnotist at an angle to the participant.

The protocol consisted of six conditions: The session started with the hypnotist asking the participant to close his/her eyes. Then, after an initial resting condition of 2 min, the hypnotist induced the four hypnotic conditions using standard texts that suggested light hypnosis, anxiety, relaxation (the latter two in reversed order for three of the seven participants), and deep hypnosis, followed by the hypnotist-controlled termination of the session that led to recovery resting. Each condition lasted for about 5 min except for deep hypnosis that lasted for about 10 min.

During the light hypnosis suggestion, the hypnotist aimed at the participants’ physical relaxation and well-being. During the deep hypnosis suggestion, the hypnotist led the participant into deep hypnosis with amnesia for his/her own name and date of birth.

After the end of the entire session, the hypnotist interviewed the participant about his/her experience during the deep hypnotic condition. Only if the participant confirmed that he/she had not been able to recall and pronounce his/her own name and date of birth, his/her data remained in the data pool.

During the entire session, multichannel EEG was recorded continuously from 19 sites on the scalp following the international 10/20 system: positions Fp1/2, F3/4, C3/4, P3/4, O1/2, F7/8, T3/4, T5/6, Fz, and Pz, using Cz as recording reference. The EEG data were amplified (band-pass 0.3–60 Hz) and digitized at 128 samples/s/channel using a Biologic Brain Atlas System (Mundelein, IL, USA).

Our analysis focused the differences of EEG microstates between light and deep hypnosis, using the experimental conditions of initial resting, light hypnosis, deep hypnosis, and recovery resting.

Data conditioning and analysis

The first 10 artifact-free 2-s EEG epochs were selected on screen from each of the four experimental conditions of initial resting, light hypnosis, deep hypnosis, and recovery. After a careful second epoch-by-epoch review for eye, muscle and movement artifacts, on the average across participants and conditions, 9.8 ± 0.19 selected epochs of 2 s (i.e. 19.6 s ± 0.38 s) of 19-channel EEG were eventually available for each participant in each of the four conditions. The selected epochs were FFT-filtered from 2 to 20 Hz and recomputed against average reference. From each multichannel EEG epoch, the single curve of Global Field Power was computed [39].

Microstate analysis: This analysis is based on viewing multichannel EEG data as a series of momentary maps of the spatial distribution of the brain electric potential on the head (potential landscapes). Such map series were found to consist of brief, subsecond time epochs of similar potential landscapes, concatenated by rapid landscape changes; these time epochs of quasi-stationary potential landscape were recognized as ‘microstates.’ Using sequential or global approaches for classification, microstates can be sorted into different classes, which are distinguished by different map landscapes [29, 37, 40]. Koenig et al. [32] analyzed data from 496 healthy subjects in a normative study and identified four classes of EEG microstates.

Microstate analysis was performed following the global approach. This approach identifies all available momentary maps that occurred at time moments of peaks of the curve of Global Field Power (from now on called ‘original maps’), and, after normalizing the maps for unity Global Field Power uses them to compute classes of maps (prototype maps) of different potential landscapes, separately for each participant and condition. This was done by modified k-means clustering [36, 40], where Global Map Dissimilarity [39] is the clustering criterion. We applied map classification into four landscape classes in order to be able to compare the present results with earlier studies [32, 36–38, 41].

We then calculated the mean maps of each condition (‘condition maps’) across the seven participants by assigning, for each participant, each of the four classes to one of four common classes across participants by determining the assignments that resulted in minimal variance across participants. These resulting four class maps for each of the four conditions (Fig. 1) were very similar to the four class prototype maps that were established in Koenig et al.’s [32] cohort of 496 normal subjects. For each of the four conditions, the four class maps were labeled following their similarity with Koenig et al.’s four class maps as microstate class ‘A,’ ‘B,’ ‘C,’ and ‘D.’

Each original map was assigned to one of the four microstate classes, using the condition maps as templates, by finding the smallest map dissimilarity between the examined original map and any of the four condition maps. A ‘microstate’ consists of the series of consecutive original maps that were assigned to the same class. Microstates of a given class can be characterized by three parameters: duration, occurrence/s, and %time coverage. The latter parameter assesses the percentage of total analysis time occupied by the microstates of a given class.

For each condition and participant, the three microstate parameters of ‘duration,’ ‘occurrence/second’ and percentage of covered total analysis time (‘%time coverage’) was computed separately for the microstates of each of the four microstate classes (A, B, C, and D). It is true that for an individual participant, the value of any one of the three parameters can be derived from the values of the two others. However, over participants this is not true anymore, and therefore the three parameters warrant separate reporting.

For each microstate, the Global Field Power peaks/s were determined, and the mean rate of the peaks/s was computed for each microstate class and experimental condition for each participant.

Power spectral analysis was done on a general level in order to examine the conditions for major effects on EEG vigilance signs: All selected 2-s EEG epochs (before band passing for microstate analysis) were subjected to FFT analysis. Integrated power was calculated in the seven independent EEG frequency bands [42] for each participant and condition: 1.5–6 Hz (delta), 6.5–8 Hz (theta), 8.5–10 Hz (alpha1), 10.5–12 Hz (alpha2), 12.5–18 Hz (beta1) and 18.5–21 Hz (beta2), and 21.5–30 Hz (beta3). The integrated power values were averaged across channels for each frequency band, experimental condition, and participant.

Statistics

The microstate parameters and the power values of the frequency bands of the four conditions were statistically

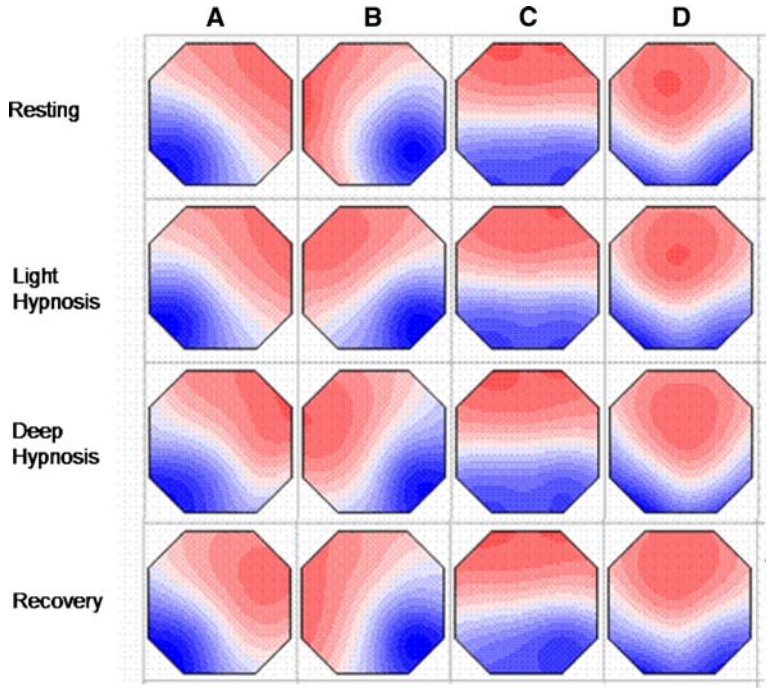

Fig. 1 Mean isopotential area-maps across participants, of the microstates of the four microstate classes (**A**, **B**, **C**, and **D**; horizontal) in the four experimental conditions (vertical) in the sequence used during the experiment: initial resting, light hypnosis, deep hypnosis, recovery. Head seen from above, nose up, left ear left; red = positive, blue = negative potential versus average of all potential values within each map (spatial DC rejection); all maps were normalized for unity Global Field Power. Note the similarity of the map landscapes within a given class across conditions; there was no significant landscape difference between conditions within any of the classes. These four observed class maps were very similar to the four class maps obtained in a large cohort of awake normals by Koenig et al. [32] and were labeled accordingly

examined using repeated-measure ANOVA's with Greenhouse-Geisser correction that were followed by *t*-tests to identify the important parameters.

The permutation statistics TANOVA [43, 44] was used to test differences between microstate potential map landscapes.

Two tail *p*-values are reported.

Results

Figure 1 illustrates the mean maps across participants of the four microstate classes for each of the four experimental conditions. For all four microstate classes, TANOVA statistics yielded no significant differences of the microstates' potential landscapes between conditions.

Figure 2 shows the mean values (and SD) across participants of the three microstate parameters for each of the four microstate classes in the four experimental conditions. Parameter-wise ANOVA's (4 microstate classes $\times$ 4 conditions) showed significant interactions for condition x class for all three microstate parameters: duration, occurrence and %time coverage ($F = 4.25$, df = 3.62, 21.7, $\varepsilon = 0.40$, $p = 0.0126$; $F = 4.59$, df = 3.01, 18.06, $\varepsilon = 0.33$, $p = 0.0002$; and $F = 5.81$, df = 3.48, 20.89, $\varepsilon = 0.39$, $p = 0.0035$, respectively).

Figure 2 also displays the results of the post-hoc tests between experimental conditions. Of all 72 post-hoc tests, 27 yielded $p < 0.05$. In deep hypnosis compared to light hypnosis, microstates of class A had significantly increased durations, more occurrences/s and more %time coverage, while initial resting and recovery showed values whose magnitude fell between those of the two hypnotic conditions. Similarly, microstates of class C showed significantly more occurrences/s and more %time coverage in deep hypnosis compared to light hypnosis (the increase in duration did not reach significance). Microstate classes B and D exhibited results in the opposite direction: significantly shorter durations, fewer occurrences/s (at $p < 0.10$) and less %time coverage in deep compared to light hypnosis, while again, initial resting and recovery showed values between the two hypnotic conditions.

When examining Fig. 2 in detail, it becomes obvious that for each microstate class, the post-hoc *t*-tests of the microstate parameters in all relevant cases (at $p < 0.10$) identified magnitude differences between conditions that all were in the same sequence of magnitude (direction); this is evidenced in Fig. 2 by the identical orientation of all

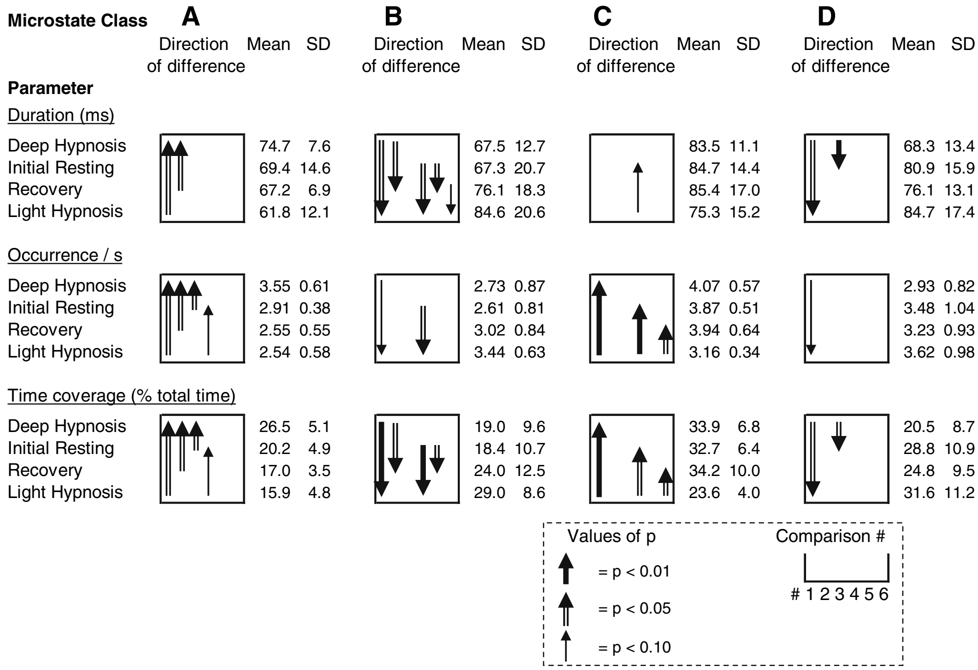

Fig. 2 Overview of the results for the microstates of the four microstate classes (**A**, **B**, **C**, and **D**): The arrows in the result boxes indicate the direction of the differences between the population mean values observed for the three microstate parameters (duration, occurrence/s, and %time coverage) in the four experimental conditions. The four experimental conditions are ranked vertically in the sequence of the magnitude of the mean values that differed at $p < 0.10$; note that this condition ranking of deep hypnosis, initial resting, recovery, and light hypnosis was identical for all three parameters. Arrows indicate the direction of the magnitude ranking of the mean values. The arrows are shown only for comparisons between conditions where the post-hoc tests yielded $p < 0.10$. Note that the directions of all arrows in each result box are upwards for class A and C, and downwards for class B and D. Note also that the listed standard deviations are not relevant for the significance of differences between conditions because paired statistics was used. The dashed rectangle displays the conventions applied for indicating the p-values of the arrows that show the direction of magnitude difference between conditions. The dashed rectangle also shows the position (horizontal) in each result box of the possible six statistical comparisons between the four experimental conditions: comparison #1 = deep hypnosis versus light hypnosis; #2 = deep hypnosis versus recovery; #3 = deep hypnosis versus initial resting; #4 = initial resting versus light hypnosis; #5 = initial resting versus recovery; #6 = recovery versus light hypnosis

arrows within a given microstate class. The sequence of relevant magnitude differences in all three parameters was either from deep hypnosis to initial resting to recovery to light hypnosis, or the inverted sequence. The direction of magnitude sequence in one direction was identical for microstate classes A and C, and in the opposite direction identical for classes B and D. Evidently, the conditions of deep and light hypnosis always are at the two ends of the observed ranges of values, with initial resting and recovery in-between, hence contradicting the expected continuum of changes from rest to light to deep hypnosis.

Figure 2 also shows that among the six comparisons between conditions that are illustrated in each result box, deep versus light hypnosis (comparison #1) as well as initial resting versus light hypnosis (comparison #4) clearly showed more relevant differences (11 and 8, respectively) than the other four comparisons (between 5 and 2).

The rate of Global Field Power peaks/s of the microstate classes showed no significant result in the overall ANOVA (4 microstate classes × 4 conditions). A parallel finding was the absence of a significant result in the overall ANOVA (7 EEG frequency bands × 4 conditions) of the power spectral values of the EEG frequency bands.

Discussion

In deep compared to light hypnosis, the three parameters of brain electric microstates showed clear differences: In contrast to light hypnosis, deep hypnosis was characterized by decreased duration, decreased occurrence/s and decreased total %time coverage of the microstates of classes B and D, while microstates of classes A and C showed the opposite behavior. The magnitude of all microstate values during the conditions of initial resting and recovery were between those for light and for deep hypnosis—i.e., initial resting/recovery resting, light hypnosis, and deep hypnosis did not constitute the expected continuum: the change from initial resting (or recovery resting) to light hypnosis was in one direction, but the change from initial resting (or recovery) to deep hypnosis was in the opposite direction.

In sum, in terms of microstate characteristics, light and deep hypnotic conditions were in opposing positions referred to the two resting conditions (initial resting as well as recovery). What is the position of the observed hypnosis results within the framework of other EEG microstate findings? As to the functional significance of classes of microstates, we observe that it is reasonable to assume that different brain potential landscapes on the head surface indicate different brain functions, because different potential landscapes must have been generated by different active neural assemblies, and different active neural assemblies most probably incorporate different brain functions. However, we are aware that the literature on the functional significance of different microstates is not very extensive and that accordingly, the following comments are quite speculative.

Decreased duration of class B and D microstates as observed during deep hypnosis is reminiscent of findings in acute, first episode schizophrenics before any medication [36, 37] and in chronic schizophrenics [41] where microstates of classes B and D also showed decreased duration. On the other hand, the present observation of increased duration of the microstates of classes B and D during light hypnosis is reminiscent of observations in very experienced mediators who showed increased duration of microstates of class B when reaching the desired optimal stage of meditation [38]. One could thus speculate that the reported ameliorating effects of hypnosis on mental functions (see Introduction) might be implemented via the properties of light hypnosis as they are reflected by the microstate parameters that run counter to those in schizophrenia, while the allegedly adverse effects of hypnosis (e.g. [45–48]) might be implemented via the properties of deep hypnosis whose microstate parameter changes resemble those in schizophrenia.

Schizophrenic states and deep hypnosis at first sight seem to be very remote from each other. There is, however, a speculative, brain functional communality between them. Schizophrenia is hypothesized to originate from impaired control/executive functions in frontal areas (e.g. [49–51]), and relatedly, hypnosis is hypothesized to be mediated by a functional dissociation of frontal and other brain areas via minimized executive initiative [52, 53], or via reduced supervisory attention [54], or via orbito-frontal suppression [14, 25]. Hypnosis imaging studies showed related results in fMRI [26, 55] and to some extent in PET [3].

We noted above that the observed microstate changes from initial resting to light hypnosis resembled those from resting to meditation states [38]. Putative functional relations between hypnosis and meditation were recently discussed [56] and there were earlier suggestions that meditation might be a form of self-hypnosis; but also clear differences in subjective experience between self-hypnosis and meditation were reported [57].

Our results showed positive co-variation of the characteristics of microstate classes B and D on one hand, and of classes A and C on the other hand. For reasons of physics, the different microstate classes must reflect different organizations of brain electric activity and it is thus parsimonious to assume that they reflect different types of information processing [31, 35]. Increased versus decreased duration or %time coverage of microstates of a given class thus would imply deepened versus curtailed processing of the respective information. However, there is yet little information on the functional significance of the microstates of different classes; earlier results suggest that class A might be associated with abstract thoughts, B with visualizing thoughts [31], C with increased and D with decreased attention [58], but these tentative ascriptions are certainly incomplete and need confirmation; hence, the implications of the observed co-variation between classes remain to be clarified.

Two microstate parameters did not differentiate between light and deep hypnosis:

The landscapes of the microstate electric potential maps showed no significant differences between our four experimental conditions within any microstate class. This implies that the spatial organization of the brain processes during the hypnotic conditions did not differ grossly, suggesting quasi-constancy of the kind of information processing within a given class of microstates. However, we appreciate that the absence of a detectable difference cannot be proof for identity; also, a given potential field configuration could have been generated by many different intracerebral source geometries.

The observed, major differences in microstate characteristics between conditions indicate a curtailing or extending of the time and occurrence frequency devoted to the different types of cognitive-emotional processes; if this is so, depth of hypnosis might conceivably be implemented by precocious termination or excessive processing (and/or unrealistic differentiation) of certain types of processed information.

Also, Global Field Power peaks/s showed no significant differences between deep and light hypnosis in the four microstate classes. As this measure reflects the dominant EEG frequency, it suggests an absence of major vigilance changes between the two hypnotic conditions, and agrees with the observed lack of overall differences of EEG spectral frequency band power between the experimental conditions. But, as there is no possible proof for 'no difference,' minor differences might have become obscured by the inherent large inter-subject variability of EEG power spectra and our small number of subjects.

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