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Topographic Mapping of Rapid Transitions in EEG Multiple Frequencies: EEG Frequency Domain of Operational Synchrony

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Abstract

This paper describes for the first time the phenomenon of spatio-temporal mapping of interchannel temporal coincidences of rapid transition processes (RTPs) in multiple EEG frequencies. It is suggested that RTPs in multiple EEG frequencies found in different EEG channels could reflect the process of switching between brain operations performed by different neuronal assemblies. Systematic non-random temporal coincidences among RTPs found in those EEG channels could reflect functional (operational) synchrony. However, until now there have been no studies examining the existence of systematic RTPs synchronization among different EEG channels in a frequency domain. Therefore functional synchrony based on precise (point to point) temporal coincidence of RTPs found in different EEG channels and comparison with surrogate data were estimated. Findings of the present study demonstrated for the first time that non-random temporal coincidence of RTPs in EEG multiple frequencies exist for both closed and open eyes conditions. Each of the states had its own distinguished peculiarities. Similarity of the main peculiarities of operational synchrony found in EEG frequency domain (the present study) with EEG amplitude and phase domains (previous studies) permitted us to conclude that operational synchrony is a universal phenomenon in brain activity. Therefore, patterns of interaction between the cortical areas, which are usually calculated with classical cross-correlation and coherence analysis, may be complemented with operational synchrony.

Key words: Electroencephalogram (EEG); Frequency domain; Multiple brain oscillations; Short-term spectral patterns; Functional synchrony and Connectivity; Metastability and Brain operations.

List of abbreviations:

EEG – Electroencephalogram

RTPs – Rapid transition processes

SC – Synchronocomplex

SP – Spectral pattern

1. Introduction

At present it is well established that an electroencephalogram (EEG) is a highly non-stationary signal (Bodenstein and Praetorius, 1977; Barlow, 1985; Jansen and Cheng, 1988; Shishkin et al., 1997; Kaplan, 1998; Kaplan et al., 2005) and may be considered to be the result of “gluing” of short-term stationary casual processes with different probability characteristics (a piecewise stationary) (Brodsky et al., 1999; Fell et al., 2000). Considering that an EEG signal is characterized by three major components (amplitude, frequency and phase), one may assume that each of them can exhibit non-stationary behavior. Indeed, it has been demonstrated that all three EEG characteristics change abruptly with the progression of time (for EEG amplitude see: Fingelkurts et al., 2004; Kaplan et al., 2005; Fingelkurts and Fingelkurts, 2008, 2010a; for EEG frequency see: Fingelkurts et al., 2003a,b; for EEG phase see: Freeman, 1990, 2004; Wallenstein et al., 1995; Kozma and Freeman, 2002; Puljic and Kozma, 2003). In other words, the values of EEG amplitude, frequency and phase persist for some time around some stable average, then abruptly “jump” up or down to a new stable average which after some time is replaced by another average level. These “jumps” in EEG characteristics or rapid transitional periods (RTPs) as we named them (Fingelkurts and Fingelkurts, 2001, 2008) mark the boundaries of segments of relatively stable brain functioning. It has been proposed that during these stationary periods a particular brain system (transient neuronal assembly) executes separate operations (for a review see Fingelkurts and Fingelkurts, 2005). Neuronal assembly is defined as a set of neurons that cooperate (synchronize their activity) to perform a specific computation (operation) required for a specific task (Palm, 1990; Eichenbaum, 1993; von der Malsburg, 1999; Buzsáki, 2006). The abrupt transition from one EEG segment to another in this sense reflects the changes of transient neuronal assembly state or changes in the activity of the two or more of such assemblies (Lehmann, 1971; Jansen and Cheng, 1988; Kaplan et al., 2005). This suggests that ongoing brain activity occurs in discontinuous steps (Freeman, 1990, 2004; Freeman and Holmes, 2005; Kozma and Freeman, 2002; Kozma et al., 2005) and confirms the view that the cerebral cortex is continuously active even in wakefulness (Thatcher and John 1977; Herscovitch 1994; Arieli et al., 1996; Tsodyks et al., 1999; Raichle et al., 2001; Raichle and Snyder, 2007).

Studies on EEG amplitude domain (for the reviews see Fingelkurts and Fingelkurts 2001, 2005, 2008, 2010a) and EEG phase domain (Freeman and Rogers, 2002; Freeman and Holmes, 2005; Kozma et al., 2005) demonstrated that (a) RTPs observed in different EEG channels systematically coincide in time and (b) this RTP temporal synchronicity is not occasional, it occurs significantly higher or lower than is expected by chance alone. The RTP synchrony estimates periods of the mutual temporal stabilization of quasi-stationary segments in the multichannel EEG (Fingelkurts et al., 2005). At the neurophysiological level this implies that various neuronal assemblies located in different cortical regions synchronise their operations on a particular time-scale (Freeman and Holmes, 2005; Fingelkurts and Fingelkurts, 2005). Such synchronization reflects brain functional connectivity (as it is defined by Friston et al., 1993, 1996) and was named Operational Synchrony (Fingelkurts and Fingelkurts, 2001).

Although it is often claimed that volume conduction is the main obstacle in interpreting EEG data in terms of brain connectivity, it has been shown previously through experimental studies that in contrast to many other measures of functional synchrony, brain connectivity measure based on temporal coincidences of RTPs is sensitive to the morpho-functional organization of the cortex rather than to the volume conduction and/or reference electrode (for relevant details, we refer the reader to Kaplan et al., 2005; Fingelkurts and Fingelkurts, 2008). These findings also suggested the existence of statistical heterogeneity (anisotropy) of electromagnetic field in regard to the processes of mutual stabilization of quasi-stable periods in regional EEGs. In addition and contrary to other EEG measures of functional connectivity, the measure based on temporal coincidences of RTPs does not require implicit or explicit source model for the interpretation of its results (Fingelkurts and Fingelkurts, 2001). Additionally, there have been actual cases (for the review see Fingelkurts and Fingelkurts, 2010b) where electrode-functional source correspondence was seen in studies focusing on the cortical activities immediately under the skull thus suggesting that local EEG is sensitive to morpho-functional organization of the cortex: (1) Covariance between neighboring electrodes across cortex functional boundaries (e.g., parietal to temporal areas) is much smaller than covariance within functional regions (e.g., left parietal to midline parietal area), indicating that multiple distinct functional areas are assessed by topographic EEG (Kooi, 1971; Bullock and McClune, 1989). (2) Experimental findings demonstrated that the probabilities of firing of neurons observed singly and in small groups simultaneously are in close statistical

relationship to the EEG recorded in the near vicinity (Freeman, 1975; Eeckman and Freeman, 1990, 1991). Therefore the EEG can provide an experimental basis for estimating the local mean field of contributory neurons. (3) Important work came from Cook et al. (1998) who demonstrated experimentally the accuracy of topographic EEG mapping for determining local (immediately under the recording electrode) brain activity. Study demonstrated that there are statistically significant linear relationships between EEG power and perfusion in the majority of frequency bands (Cook et al., 1998). This finding is in line with earlier study of Inouye et al. (1986), where the authors demonstrated that endogenous EEG activity originated from underlying cortex area contributes the most to the spectral power measured from the given EEG electrode. Whereas exogenous EEG activities originated from the other cortical areas contribute to spectral power of the same EEG electrode insignificantly. Thus, together described works suggest that topographic EEG mapping can accurately reflect local brain function and that it is comparable to other topographic methods.

Notice that in these studies there are no inferences about *primary* generators (sources) of the EEG activity in different cortex areas. Considering that all activities (influences) from multiple primary sources are not just mixed, summed or averaged in a given cortex area, but are integrated within the current state (activity) of this area, the local EEG is considered to represent a functional source, which is defined as the part or parts of the brain that contribute to the activity recorded at a single sensor (Stam, 2005; Wackermann and Allefeld, 2007). A functional source is an operational concept that does not have to coincide with a well defined anatomical part of the brain, and is neutral with respect to the problems of localization of primary source and volume conduction (Stam, 2005; Wackermann and Allefeld, 2007).

Until now there have been no studies examining the existence of systematic RTPs synchronization among different EEG channels in a frequency domain. At the same time, exactly different frequencies of EEG oscillations reflect functionally different components of information processing acting on various temporal scales (Klimesch et al., 2005). It is suggested that the oscillatory activity of neuronal pools, which is reflected in characteristic EEG rhythms, constitutes a mechanism by which the brain can regulate changes of a state in selected neuronal networks to cause qualitative transitions between modes of information processing (Lopes da Silva, 1996). Hence, different oscillatory patterns may be indicative of different information processing states, and it has been proposed that the oscillatory patterns play an active role in these states (Bhattacharya, 2001; Lakatos et al., 2005).

Various EEG oscillatory patterns can be indexed by different types of short-term EEG spectral patterns (SPs) – a distribution of spectral power values (Fingelkurts et al., 2003a), where each SP type may be considered as a single event in EEG phenomenology (Fingelkurts and Fingelkurts, 2010b). It was demonstrated that even at rest the EEG SP types emerge, persist for some time and then disappear to be replaced by other SP types (Fingelkurts et al., 2003a,b). Additionally, the dynamics of spatio-temporal variability of resting EEG short-term SPs was characterized by abrupt alteration of relatively stable periods, the duration of which were significantly different from the respective characteristics of a random process (Fingelkurts et al., 2006). The obtained results suggest an existence of a special operational synchrony within basic EEG rhythms. In contrast to classical synchronization methods (coherence, correlation, phase and others), this kind of synchrony reflects a temporal consistency of quasi-stationary modes of brain oscillatory activity.

Currently, a number of EEG measures of integrative brain activity indexed by functional connectivity are available. They are: (1) correlation and coherence coefficients (for the reviews, see Thatcher et al., 1986; Nunez et al., 1997) as well as partial directed coherence (Baccala and Sameshima, 2001); (2) dynamic imaging of coherent sources (Gross et al., 2001), and phase synchrony based on wavelet (Lachaux et al., 1999) or Hilbert (Tass, 1999) transforms; (3) indices of mutual information (Xu et al., 1997); (4) “geometric” estimations of joint coordination of local EEGs calculated with the help of factor analysis (Manmaru and Matsuura, 1989; Lazarev, 1997) and multivariate linear regression (Wada et al., 1996; Lehmann et al., 1995) of the primary EEG characteristics; (5) chaotic dynamics of an EEG vector composed of simultaneous momentary counts of local EEGs (Matousek et al., 1995); (5) spectro-correlative characteristics of local EEGs (Ivanitski et al., 1990; Sviderskaya and Korol’kova, 1997); and (6) spatially oriented segmentation of cortical potentials proposed by Lehmann (Lehmann, 1971, 1987).

Even though, many of these approaches have proved to be useful for characterization of integrative brain activity, all of them have one or more drawbacks and limitations from the following list (for the critical and detailed discussion, see Fingelkurts et al., 2005; Fingelkurts and Fingelkurts, 2005): Such methods (1) are designed predominantly for EEG analysis only in pairs of derivations, (2) do not take into consideration the non-stationary nature of the signal, (3) indicate only the linear statistical link between time-series curves in a frequency band, (4) require long time epochs of analysis, (5) can be applied only to homogeneous

medium, which is an unrealistic assumption for the brain, (6) borrow complex methodologies and conceptual frameworks from physics, mathematics, and engineering, but use them loosely when applying to the analysis of physiological signal, (7) as very averaged indices they lose a substantial part of their diagnostic value for studying discrete functional states of the brain, (8) local EEGs participate in the formation of the resulting dipole vector far from equally, what is unjustified from the viewpoint of indubitable neurobiological equivalence of cortical areas, (9) the measures used to characterize the EEG are often difficult to interpret in terms of their physiological correlate, (10) all existed measures of brain functional connectivity do not directly estimate metastability in the brain (Fingelkurts and Fingelkurts, 2004).

Additionally, lack of initial “attachment” of the majority of the abovementioned measures to brain oscillations makes results ontologically unpromising. At the same time, different frequencies of brain oscillations reflect functionally different components of information processing acting on various spatial scales (Klimesch et al., 2005). It is supposed that brain functioning is based on short- and long-range interactions between neuronal assemblies which oscillate at multiple frequencies (Jing and Takigawa, 2000; Bhattacharya, 2001) which are coherent and specific and thus capable of resonance – functional communication (Basar et al., 2001).

Therefore, it was proposed to combine the advantages of the temporal and frequency approaches for the analysis of segment-to-segment organization of the cortical biopotential field. In such a way, this approach results in the topographic map of the EEG SP transitions and thus, enables researches to study spatio-temporal variability of brain oscillatory states (indexed by short-term spectral descriptions) in multichannel EEG. This analysis of topographic SP variability may permit researches to trace episodes of the metastable cortical inter-area cooperations independently on partial correlation and/or coherency between the local EEGs. Additionally, this method requires no a priori assumptions about which frequency bands should be synchronised, but rather relies on the natural statistical properties of the data.

In context of the aforementioned it is reasonable to study episodes of synchrony within the dynamics of the spatial mosaic of different EEG oscillations. Hence, the aim of this study was to investigate systematic temporal coincidences of RTPs in EEG oscillatory patterns

(indexed by EEG SP types) in a broad frequency range (0.5–30 Hz) among different EEG channels.

2. Materials and methods

2.1. Subjects

Twelve healthy, right-handed adult male volunteers (aged 19–26) participated in the study. None of the subjects reported any history of brain traumas or concussions, neurological or psychiatric disorders, acute or chronic medical illness, or was on medication at the time of the EEG registration. In addition, all of them have normal blood pressure and pulse rate.

All of the subjects were informed beforehand about the nature of the procedure. Written, informed consent from all subjects and institutional ethical committee approval were obtained prior to the experiment. The study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Since alcohol influences variation of normal EEG (Propping et al., 1980), subjects were asked to abstain from alcohol for 2 days before EEG registration. To control variation due to food intake, participants were asked to have breakfast with two slices of toast, jelly and orange juice, and were instructed to avoid caffeine for 12 h prior to the recordings.

The EEG registrations began at 10:00 a.m.

2.2. Procedure and data acquisition

Eight Ag/AgCl electrodes were placed bilaterally on the subject's scalp using the 10/20 system of electrode placement at O₁, O₂, P₃, P₄, C₃, C₄, F₃ and F₄. Vertical and horizontal electro-oculograms were recorded. All electrodes were referred to linked ears (linked-ears reference was obtained digitally from two separate, impedance-checked channels). Raw EEG signals were amplified and bandpass-filtered in the 0.5–30 Hz frequency range and digitized at a sampling rate of 128 Hz by a 12-bit analog-to-digital converter with a resolution of 1 μ V/bit. This frequency range was chosen because approximately 98% of spectral power lies within these limits (Thatcher, 2001).

Even though frequencies above 30 Hz (gamma band) have been proposed to be functionally informative, there are a number of methodological issues which lead us to exclude frequencies above 30 Hz from the present analysis: (a) it was shown, that there is little effect of volume conduction on the shape of the spectrum below about 25 Hz and spatial filtering is significant only for frequencies above 25 Hz (Robinson et al., 2001); (b) high-frequency spindles have very low signal-to-noise ratio, what results in considerable contamination of gamma band by noise; (c) dynamics of high-frequency responses may be a trivial by-product of power changes in lower frequencies (Pulvermuller et al., 1995) and/or due to ringing of filters by EEG spikes recurring at theta rates (Freeman, 2003); (d) gamma oscillations are present during states such as deep anesthesia, where conscious cognitive processing is absent (Steriade and Amzica, 1996; Steriade et al., 1996); (e) it was demonstrated that some of the induced gamma activity that was attributed to feature binding generated in visual cortical areas were in fact artifacts of miniature saccades evoked by the stimuli (Yuval-Greenberg et al., 2008). In addition, a strong link between gamma band oscillations and (un)conscious facial muscle activity during cognitive tasks was confirmed by showing that such oscillations disappear despite normal cognitive performance when the muscles are paralyzed (Whitham et al., 2007, 2008; Ball et al., 2008); (f) comprising only 2% of spectral power (Thatcher, 2001), contribution of high-frequency band into spectrum cannot be significant; (g) Bullock et al (2003) demonstrated many “good” rhythms in the 2–25 Hz range which were mainly sinusoidal, but did not find them in 30–50 Hz band; (h) gamma band is often known to carry cognitively relevant information, however presented study was conducted during resting conditions. Considering all of these, there might be difficulties in the meaningful interpretation of effects in high-frequency band regardless of how powerful or statistically significant they may be.

The impedance of the recording electrodes was always below 5 k Ω . The presence of an adequate EEG signal was determined by visual inspection of the raw signal on the computer screen.

After the electrodes were placed on the subject’s head and the instrument calibrated, the subject was seated in a comfortable chair in a registration room and the procedure was explained. To reduce muscular artefacts in the EEG signal, the subject was instructed to assume a comfortable position and to avoid movement.

Instructions designed to minimize movement and relax jaw muscles resulted in suppressing the myogram class of artifact to the extent that the high-frequency spectrum was not significantly affected. A subject was instructed also to look straight in front of him/her (even when the eyes were closed) and to avoid unnecessary eye movements. Constant visual EEG monitoring allowed the selection of only artifact-free 1-min EEG recordings for analysis.

Alertness of subjects during the EEG recording was determined by the design of the study: separate 1-min EEGs were recorded in a relatively well-lit room with a short break in-between to assume a comfortable position. Such design should keep subjects awake. Vigilance of subjects was controlled by visual detection for the presence of sleep spindles which appear naturally during drowsiness (Rechtschaffen and Kales, 1968). None of the subjects demonstrated sleep spindles in the recorded EEGs.

For each subject ten 8-channel 1-min EEGs were recorded randomly during steady resting conditions for closed and open eyes separately. Such ongoing EEG activity during resting condition reflects the current functional state of neuronal masses rather than a random process (Livanov, 1984). A total of 102 (for closed eyes) and 45 (for open eyes) artifact-free 1-min EEGs were selected for the analysis.

According to literature two one-min EEGs have proven to produce reliable estimates of internal consistency (Coan et al., 2001). Moreover, even the duration of 20 sec of EEG epoch is sufficient to reduce adequately the variability inherent in the EEG (Gasser et al., 1985). In the present study majority of the subjects contributed to EEGs' pool with 10 one-min EEGs (for closed eyes) and 4 one-min EEGs (for open eyes), which is well above the aforementioned limits.

2.3. Data Processing

EEG analysis was undertaken in four stages (Fig. 1). Since EEG is widely referred to as a non-stationary signal with varying characteristics (for the reviews see Barlow, 1985; Jansen and Cheng, 1988; Kaplan, 1998; Kaplan et al., 2005), EEG oscillations are expected to be dynamic in nature. During the first stage of EEG analysis the data series were divided into overlapping windows in order to capture EEG changing dynamics. EEG oscillations were

quantified by calculation of individual short-term EEG SPs. *Individual power spectra*¹ were calculated in the range of 0.5–30 Hz with 0.5-Hz resolution (61 values), using FFT with a 2-sec Hanning window shifted by 50 samples (0.39-sec) for each channel of 1-min EEG. According to previous studies, these values proved the most effective for revealing oscillatory patterns from the signal (Levy, 1987; Kaplan, 1998).

The works which have studied the effect of epoch length on the variability of power spectrum (Levy, 1987; Kaplan, 1998) demonstrated that (a) the epoch-to-epoch variability with power spectra computed using 2-sec epochs was significantly less than the variability when power spectra were computed using longer epoch lengths, and (b) analysis using 2-sec epochs identified changes more rapidly than analysis using any longer epoch length, and the differences were clinically significant as well. Moreover, a 2-sec epoch is long enough to get a reliable estimation of the lowest frequency (0.5 Hz), and is short enough to be quasi-stationary (McEwen and Anderson, 1975; Inouye et al., 1995). Taken together these findings suggest that 2-sec epoch lengths are preferable when power spectrum analysis is used.

Further, according to the work of Kaplan (1998) in which the author studied the effect of window shift on disclosing oscillatory patterns from the signal using shifts from 1 to 256 samples, the window shift in 50 samples was the most effective. Sliding spectral analysis with overlapping segments, previously applied to EEG signals (Keidel et al., 1987; Tirsch et al., 1988), (a) takes the non-stationarity of the time series into account, (b) compensates for the effects of windowing and (c) prevents loss of information due to residual activity.

We did not use predefined and isolated from each other narrow frequency bands because by doing so we could not examine behaviour of the actual/natural composition of brain oscillations involved. Earlier it was demonstrated that brain functioning is represented by multiple oscillations (Basar et al., 2000). According to the superposition principle introduced by Basar et al. (1999), brain activity is accompanied by superimposed multiple brain oscillations in many frequency bands (for the review, see Basar et al., 2004).

¹ Log transformation of the power spectra was not used in the present study for the following reason: Log transformation usually normalizes a power spectrum, but, at the same time, it artificially reduces the contrast of the differences between large and small power values. This leads to the increased contribution of the small-amplitude values and correspondently, the noise into a total spectrum. For the purpose of this paper “clean” power spectra without noise contamination are of great importance. Additionally, log transformation can exaggerate extremely small, but topographically reproducible errors in areas with low EEG power.

After calculation of EEG short-term SPs, the total number of individual SPs for each channel of one-min EEG was 149 (Fig. 1). Each SP was labelled according to the index of the class to which it belongs with the help of a probability-classification analysis of the short-term EEG SPs (see Appendix to this article). Sequential single EEG SPs were adaptively classified in each channel of 1-min EEG using a set of standard SPs, which were generated automatically from the EEG data itself – and was not chosen arbitrary. The number of SPs classes in this study was 18–26 (for different EEG channels) (see Appendix to this article). As the result of classification procedure, each current SP was labelled according to the index of the class to which it belongs. Hence, each EEG signal was reduced to a sequence of individually classified SPs (Fig. 1).

During the second stage, *segmentation of EEG signal* based on the changes of SP type was performed (Fig. 1). A single EEG spectrum illustrates the particular integral dynamics of tens and hundreds of thousands of neurons in a given cortical area at a particular point in time (Dumermuth and Molinari, 1987). Therefore, the absence of variance of a single SP type during several analyzed epochs proves that in a given cortical area the same macro-regimen of neuronal pool activity is maintained throughout that period. Thus, periods of several consecutive EEG epochs which are characterized by the same SP type comprise a SP-segment – EEG segment of quasi-stationary oscillatory activity. The moment of change of the type of SP-segment marks a RTP. In such a way, time coordinates of each RTP for each EEG channel separately were determined (Fig. 1). The theoretical concepts behind segmentation analysis of EEG are described elsewhere (for the reviews see Fingelkurts and Fingelkurts, 2001, 2008; Kaplan et al., 2005).

During the third stage, *functional brain connectivity* based on temporal coincidence² of RTPs found in different EEG channels was estimated (Fig. 1). The number of RTP's temporal coincidences was counted for each 1-min EEG and compared with that of surrogate data. Two (or more) EEG channels were considered functionally connected if systematic temporal relationship among them (the number of coincided RTPs per 1-min EEG) was different from random level measured in surrogate data (see below). The values which are statistically

² Technically, two (or more) RTPs from different EEG channels were considered coincident temporally when these RTPs had the same temporal coordinates. However, position of temporal coordinate of a given RTP is dependent on a discrete temporal lag of 0.39s used for calculation of SPs (see above). Therefore, the actual temporal coincidence is occurred in 0.39s window. Considering that the shift in 0.39s was the most effective on disclosing oscillatory patterns from the signal in modelling study (Kaplan, 1998), one may assume that measured temporal coordinates of RTPs are approach the real ones.

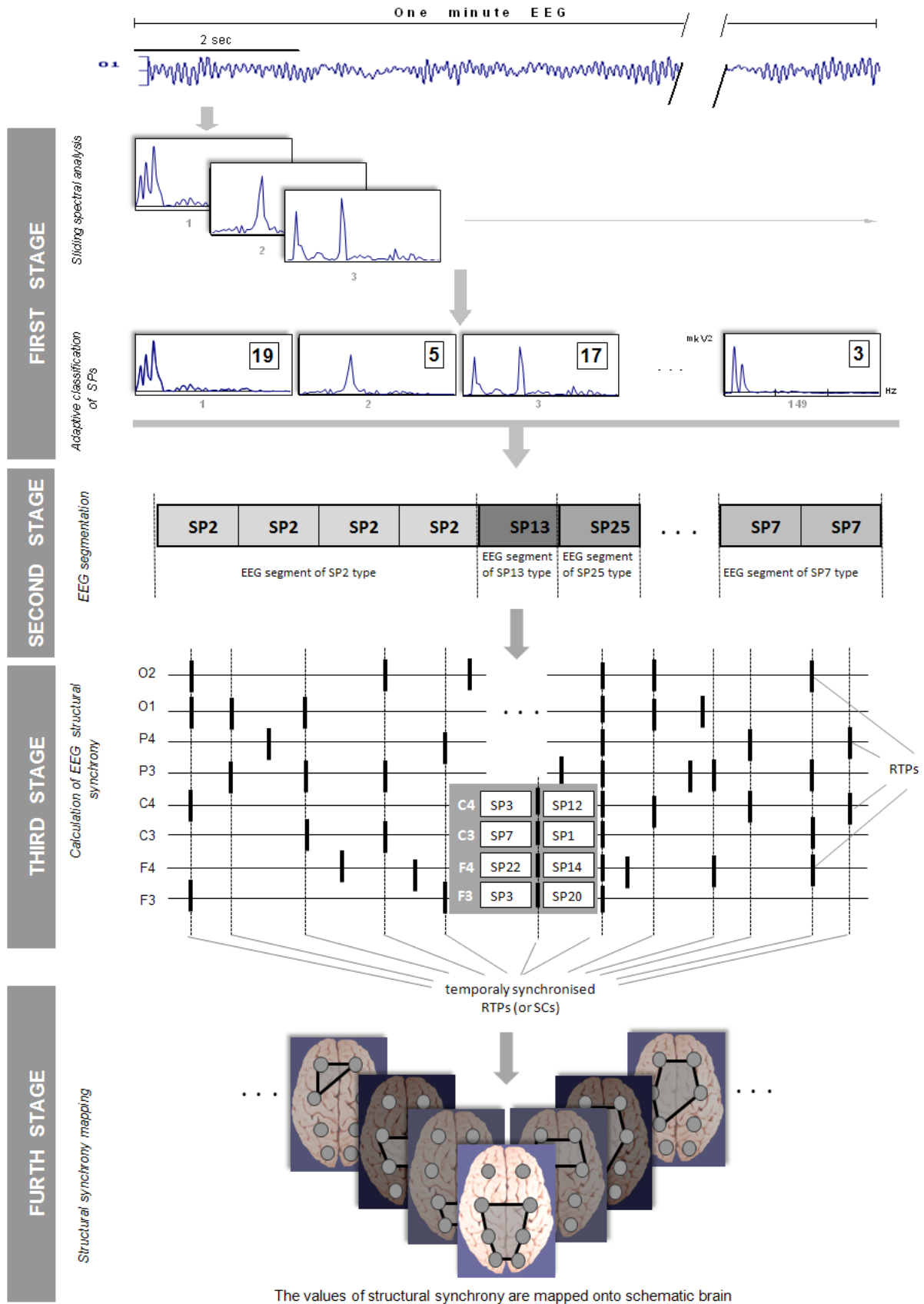


Figure 1. The scheme of the data processing. *First stage:* Sliding spectral analysis and adaptive classification of short-term spectral patterns (SP) were done separately for each subject and each channel of 1-min EEG. O1 = Left occipital EEG channel. Gray small numbers under each SP represent the running numbers from 1 to 149 of EEG epoch analysis. The number in the square represents the class to which a given SP was assigned during classification procedure. *Second stage:* Segmentation of EEG signal based on the changes of SP type was performed. The moment of change of type of SP-segment marked a rapid transitory period (RTP). In such a way, time coordinates of each RTP for each EEG channel separately were determined. *Third stage:* Functional connectivity based on precise (point to point) temporal coincidence of RTPs found in different EEG channels was estimated. *Fourth stage:* EEG structural synchrony mapping was performed based on mapping onto schematic brain maps synchronised EEG channels (synchrocomplexes) by connecting lines between the EEG channels involved.

significantly above the random level indicate ‘active’ coupling of EEG segments (synchronization of EEG segments is observed significantly more often than it expected by chance), whereas the values which are statistically significantly below the random level indicate ‘active’ decoupling of EEG segments (synchronization of EEG segments is observed significantly less than it expected by chance).

Notice that synchronised RTPs mark transitions between different types of SPs, which are usually different in various EEG channels (Fig. 1, third stage, insertion). Therefore, described RTPs-based measure of functional connectivity, in contrast to conventional approaches, is free from similarities of the EEG signals in different channels. In this context, stabilization of SP RTPs simultaneously in several cortical areas may reflect formation of steady cooperation between cortical areas independently on particular characteristics of these SPs within each EEG channel.

Result of such cooperation represents a metastable state (Kelso, 1995; Bressler and Kelso, 2001; Kozma et al., 2005; for the recent reviews on metastability in the brain, see in Fingelkurts and Fingelkurts, 2004, 2005, 2008 and Werner, 2007). It was suggested that this measure reveals functional (operational) interrelationships between cortical sites different from those measured by correlation, coherence and phase analysis (Kaplan et al., 2005; Fingelkurts et al., 2005). From a qualitative perspective, the coupling of EEG segments corresponds to the phenomenon of synchronization of brain operations or operational synchrony – OS (Kaplan et al., 1997; Fingelkurts and Fingelkurts, 2001, 2004, 2005, 2008).

Each case of temporally synchronised RTPs between two or more EEG channels is described as a synchronocomplex (SC). The number of cortical areas recruited in SC is described as “the order of areas recruitment.” All SCs were divided into seven categories based on the number of cortex areas involved: SC₂ – SC with 2nd order of area recruitment, SC₃ – SC with 3rd order of area recruitment, SC₄ – SC with 4th order of area recruitment, SC₅ – SC with 5th order of area recruitment, SC₆ – SC with 6th order of area recruitment, SC₇ – SC with 7th order of area recruitment and SC₈ – SC with 8th order of area recruitment. Notice that any given SC was considered as a member of its own category (for example, SC₃) only if correspondent RTPs coincided in time among correspondent number of EEG channels (in this example, 3). However, any three SC₂s which could comprise the SC₃ but which did not coincide in time between each other were not considered as producing SC₃ type and, therefore was not counted. The same logic was applied for any SCs and for any category.

At stage four, *EEG structural synchrony mapping* was performed (Fig. 1). The most frequent SCs which occurred (a) in the largest number of repetitions (in %) among all found SCs ($n = 14156$ of all SCs for closed eyes and $n = 6195$ of all SCs for open eyes) and (b) in more than 40% of all EEGs ($n = 102$ for closed eyes and $n = 45$ for open eyes) were mapped onto schematic brain maps as connecting lines between the EEG channels involved.

2.4. Control for a non-random RTP synchrony

Control for a non-random RTP synchrony was performed by comparing results of synchrony from real EEG with those of surrogate data:

Surrogate data: Surrogate data were used to control for the neural origin of spatial-temporal dynamics of SPs, which is commonly applied as direct probing a signal for a non-random spatial-temporal structure (Ivanov et al., 1996). Surrogate signals have identical parameters with the original signals but do not have spatial-temporal correlations. Construction of surrogate data is illustrated in figure 2.

In order to simulate a situation with full temporal mismatch, 8 channels of the initial 1-min EEGs were mixed such that no two channels were recorded at the same time in each of the newly constructed 8-channel 1-min EEGs. This way, the natural time relations between channels in surrogate EEG were completely destroyed; however, the natural dynamics of SP-

segments sequence and the ratio between different types of SP-segments within each EEG channel remained the same (Fig. 2).

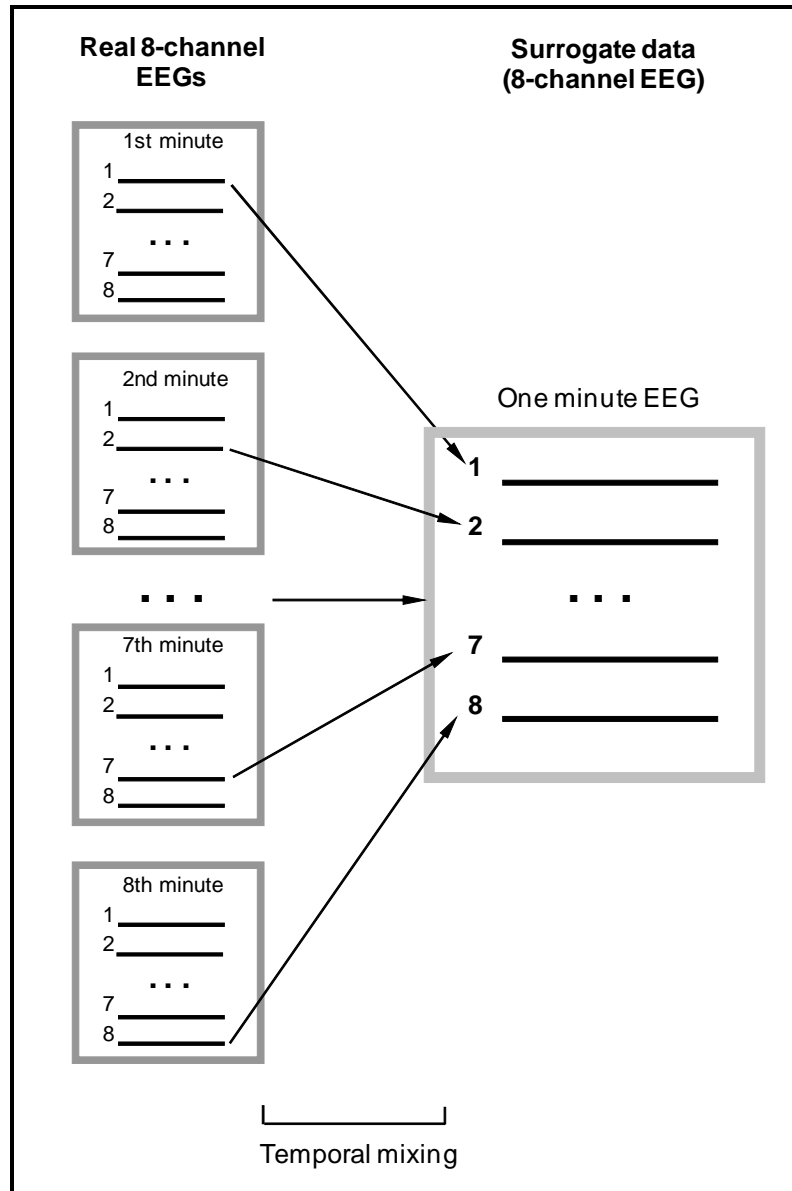


Figure 2. Construction of surrogate data: only one channel from each real 8-channel EEG (one minute) was mixed into surrogate 8-channel EEG (one minute). Thus, mixing of the real EEG channels was done in such a way that each channel of surrogate EEG was recorded in a different time.

2.5. Statistics

In order to reveal statistically significant differences between closed eyes and open eyes conditions, and surrogate data the Wilcoxon matched pairs t -test was used. Statistical significance was assumed when $p < 0.05$ (only statistically significant values are displayed).

3. Results

3.1. EEG functional (operational) connectivity

EEG segmentation revealed that EEG channels were characterised by 30 to 114 RTPs (average values for each EEG channel for closed and open eyes separately are presented in Table 1). In general, open eyes condition had more RTPs per EEG channel than closed eyes condition ($p < 0.008$) with larger difference in the posterior part of the head. After RTPs in EEG multiple frequencies (indexed by the change of the type of SP-segments) were determined in each EEG channel, the absolute number of RTP' temporal coincidences between different EEG channels (or SCs) was calculated. There was no statistically significant difference between the total number of SCs for closed and open eyes conditions (see insertion in Fig. 3).

Table 1. Average number of RTPs for each EEG channel for each condition separately.

Data averaged across all one-minute EEGs of all subjects ($n = 102$ for closed eyes and $n = 45$ for open eyes). Data presented as mean \pm standard deviation.

	O2	O1	P4	P3	C4	C3	F4	F3
Closed eyes	74.2 \pm 17.9	78.7 \pm 16	82.3 \pm 15.5	82.5 \pm 14.3	85.2 \pm 16.7	84.1 \pm 17	85.5 \pm 17.9	85.9 \pm 15.8
Open eyes	82.9 \pm 14.2	83.6 \pm 13.3	88.2 \pm 11.7	88.8 \pm 12.3	87.6 \pm 12.4	89 \pm 12.8	85.8 \pm 13.4	87.9 \pm 14.9

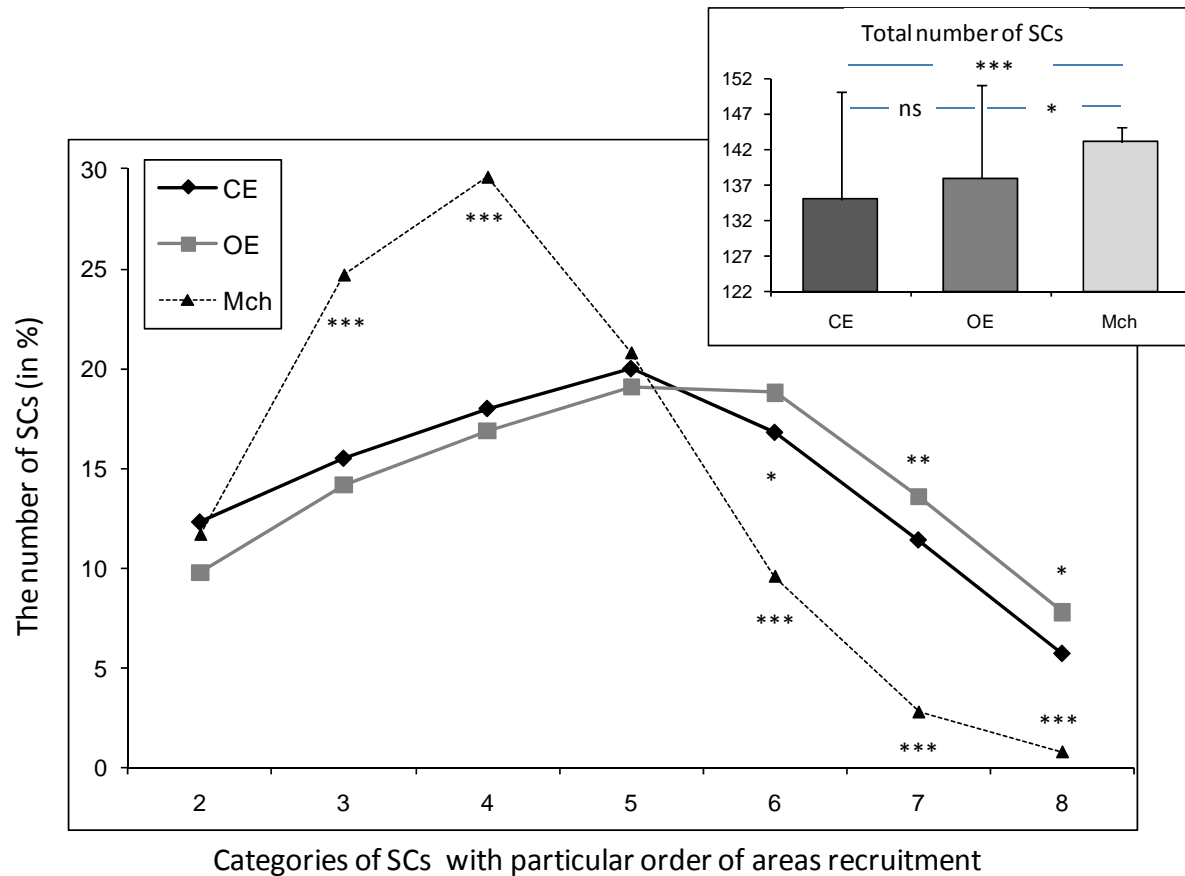


Figure 3. The number of synchrocomplexes (SCs) within each category (in % from the total number of SCs in one-minute EEG). In the insertion the total number of SCs per one-minute EEG is presented. Data averaged across 102 EEGs (for closed eyes - CE) and 45 EEGs (for open eyes - OE). MCh = mixed channels (surrogate data); ns = statistically nonsignificant; * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$

At the same time, these two conditions differed from each other by the number of SCs within each of the seven categories (see Section 2.3) (Fig. 3). Figure 3 illustrates percent distribution of SCs among all SC categories. The closed eyes condition was characterised by a larger percent of SCs with 2nd, 3rd, 4th and 5th order of areas recruitment (not statistically significant) and by smaller percent of SCs with 6th, 7th and 8th order of areas recruitment when compared with open eyes condition ($p < 0.05$ to $p < 0.01$). Moreover, for the closed eyes condition SCs with 5th order of areas recruitment was characterised by the largest percent of SCs, whereas for the open eyes condition number of SCs was the largest for SCs with 6th order of areas recruitment (Fig. 3).

To what extent do these estimations reflect the functional cortical inter-regional cooperation? It is obvious, that even in the absence of any functional interrelation between the EEG channels there should be a certain random level of RTPs synchronisation, which would reflect merely occasional combinations of RTPs from different channels.

Figure 3 depicts the number of SCs from the surrogate data, in which the inter-channel correlation is completely absent whereas the regularities of SP-segments sequence within each channel remain unchanged. It is evident that, both the number of SCs in EEG (insertion in Fig. 3) and the distribution of SCs among different categories in surrogate data (Fig. 3) were statistically different ($p < 0.05$ to $p < 0.001$) from real EEG (closed and open eyes conditions). The number of SCs from the categories with 3rd and 4th order of area recruitment was significantly smaller for both conditions than for the surrogate data. At the same time, the number of SCs from the categories with 6th, 7th and 8th order of area recruitment was significantly larger for both conditions than for the surrogate data (Fig. 3).

Taking into account that the process of functional cortical inter-regional cooperation in EEG frequency domain is a real phenomenon it is reasonable to look further into the details of the process. Were different EEG channels equally participating in the synchronization process? Figure 4A illustrates how often each EEG channel participates in SCs. It can be seen that generally each EEG channel participated in 53–64% of SCs for both closed and open eyes conditions. Additionally, for both closed and open eyes conditions EEG channels from posterior part of the head participated in synchronisation process to a lesser extent (with the minimum for O1 and O2) than EEG channels from anterior part of the head (Fig. 4A). At the same time, closed eyes condition was characterised by smaller percent of SCs in which a given EEG channel was participating when compared with open eyes condition ($p < 0.01$).

The next issue addressed was the intensity of EEG channel's participation in the synchronization process. Figure 4B presents the number of RTPs in a given EEG channel synchronised with RTPs in any other channel or channels. It can be seen that for both closed and open eyes conditions the majority (97.7–99%) of RTPs in each EEG channel were synchronised with RTPs from other channels. At the same time, closed eyes condition in general was characterised by smaller percent of synchronised RTPs than the open eyes condition ($p < 0.04$) in all EEG channels except C3 and C4 where the situation was reversed (Fig. 4B). Again, for both closed and open eyes conditions EEG channels from posterior part

of the head were characterised by smaller values of this index (with the minimum for O1 and O2) than EEG channels from anterior part of the head (Fig. 4B).

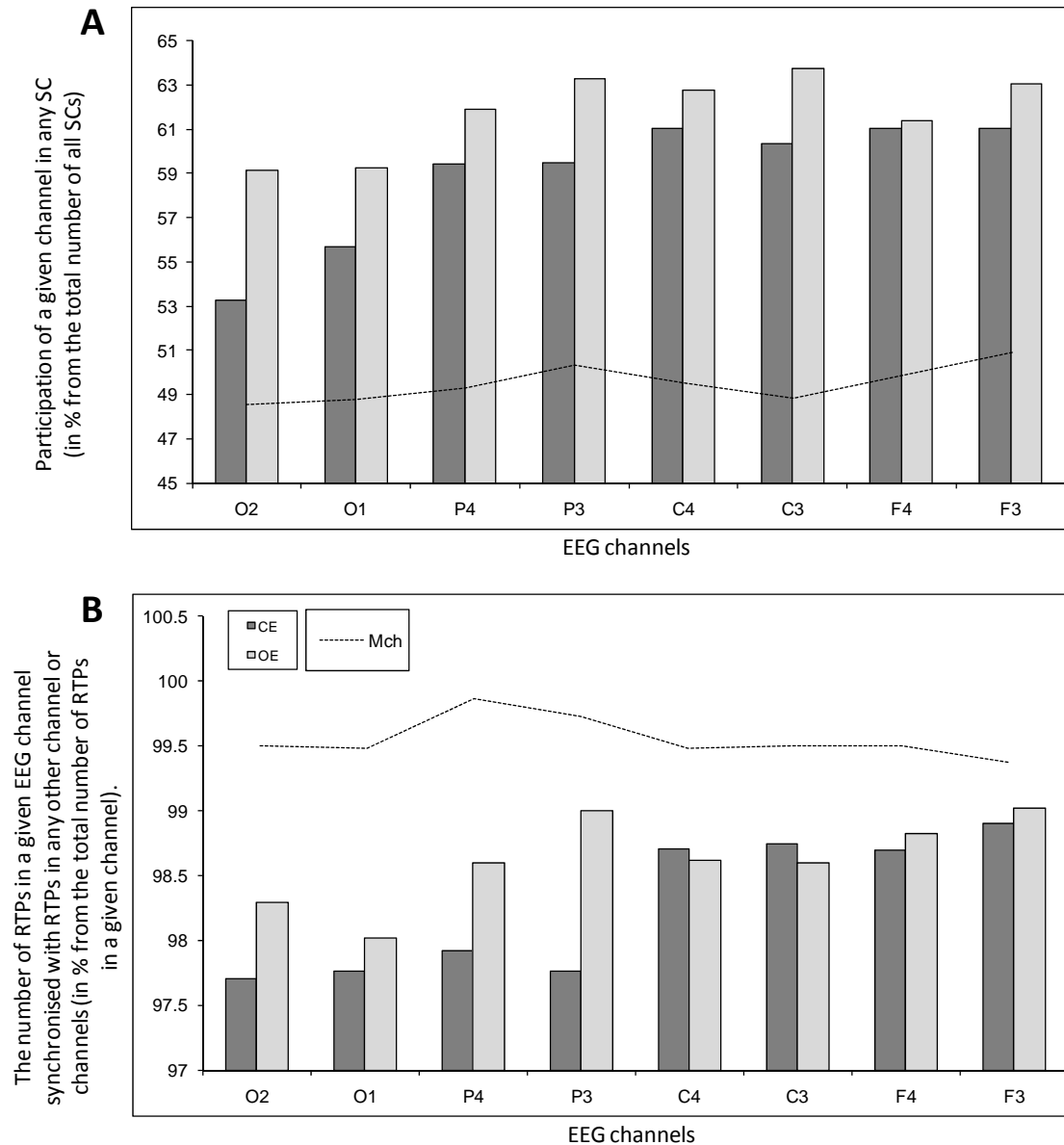


Figure 4. EEG channel's participation in synchrocomplexes (SCs) (a) and intensity of EEG channel's participation in synchronization process (b). Data averaged across 102 EEGs (for closed eyes - CE) and 45 EEGs (for open eyes - OE). MCh = mixed channels (surrogate data).

Note, that the two indices for both closed and open eyes conditions differed from those of surrogate EEG (where the natural time relations between channels were completely destroyed, however, the natural dynamics of SP-segments sequence and the ratio between different types of SPs within each EEG channel remained the same) and were statistically significant ($p < 0.01$ to $p < 0.001$; Fig. 4).

3.2. *The most representative synchrocomplexes (SCs)*

In order to choose the most frequent (representative) SCs for each of the conditions we plot the frequency of the occurrence of each SC within each category (not shown). Values were organised from smallest to largest within each category. Those SCs for which frequencies of the occurrence “jump up” more than twice from the previous values were accepted as the most frequent for any given category. Table 2 represents the most frequent types of common SCs of each category and their attributes for closed and open eyes.

It can be seen that for both closed and open eyes conditions the percent of a given SC type within each category varied between 5.9 and 22.9% (category with 8th order of areas recruitment is an exception because only one type of SC can exist for this category). Closed eyes condition for categories with higher order of areas recruitment (4, 5, 6 and 7) was characterised by higher percent of a given SC types within given categories ($p < 0.007$) when compared with open eyes condition (Table 2). For categories with lower order of area recruitment (2 and 3) the effect was reversed.

All SCs presented in Table 2 occurred in more than 40% of all EEGs for each of the conditions. Notice that both conditions were characterised by the following dependency: the higher the order of area recruitment of the SC category, the larger the percent of EEGs which were characterised by a given SC (Table 2). At the same time, closed eyes condition differed from open eyes condition by smaller percent of EEGs for SCs from the categories with 2nd, 6th and 7th order of area recruitment ($p < 0.007$).

Each of the conditions besides common representative SCs was characterised also by unique representative SCs. They are presented in Table 3.

Table 2. Most frequent types of common for closed and open eyes synchrocomplexes (SCs) of each category. Data averaged across all EEGs which had a given SC.

SC category	Combination's ID								% within category (mean \pm st.d.)	% of EEGs	
	EEG channels										
	O2	O1	P4	P3	C4	C3	F4	F3			
2	0	0	0	0	1	1	0	0	CE	11.49 \pm 8.5	44
									OE	13.7 \pm 14.2	44.4
2	1	1	0	0	0	0	0	0	CE	12.27 \pm 7.5	49
									OE	12.5 \pm 8.4	64.4
2	0	0	0	0	0	0	1	1	CE	14.91 \pm 8.9	52
									OE	11.90 \pm 6.3	53.3
3	0	0	0	0	0	1	1	1	CE	7.44 \pm 0.05	56
									OE	8.5 \pm 5.3	55.6
4	0	0	1	1	1	1	0	0	CE	6.35 \pm 3.87	51
									OE	6.5 \pm 3	48.9
4	1	1	1	1	0	0	0	0	CE	6.84 \pm 5.0	53
									OE	6.5 \pm 4.2	53.3
4	0	0	0	0	1	1	1	1	CE	7.96 \pm 0.06	71
									OE	7.5 \pm 4	62.2
5	0	1	0	0	1	1	1	1	CE	6.60 \pm 4.76	54
									OE	6.5 \pm 3.6	64.4
5	0	0	1	0	1	1	1	1	CE	6.12 \pm 0.03	66
									OE	5.9 \pm 3.5	60
6	1	1	1	1	1	1	0	0	CE	7.65 \pm 0.04	68
									OE	6.6 \pm 3.2	84.4
6	0	1	0	1	1	1	1	1	CE	8.15 \pm 0.04	64
									OE	7.1 \pm 4.3	73.3
6	0	0	1	1	1	1	1	1	CE	12.78 \pm 6.6	77
									OE	10.7 \pm 6	93.3
7	1	0	1	1	1	1	1	1	CE	22.16 \pm 0.14	87
									OE	19.4 \pm 9.6	95.6
7	0	1	1	1	1	1	1	1	CE	22.93 \pm 0.1	90
									OE	19.6 \pm 12.2	93.3
8	1	1	1	1	1	1	1	1	CE	100 \pm 0.0	100
									OE	100 \pm 0.0	100

SC = synchrocomplex; CE = closed eyes; OE = open eyes

"0" = represents EEG channels which are not functionally connected

"1" = represents EEG channels which are functionally connected

Table 3. Most frequent types of unique synchrocomplexes (SC) of each category. Data averaged across all EEGs which had a given SC.

Closed eyes

SC category	Combination's ID								% within category (mean ± st.d.)	% of EEGs
	EEG channels									
	O2	O1	P4	P3	C4	C3	F4	F3		
2	0	0	1	1	0	0	0	0	13.32 ± 11.7	39
3	0	0	0	0	1	1	1	0	8.01 ± 5.6	40
3	0	1	0	0	0	0	1	1	7.57 ± 3.57	47
3	1	1	1	0	0	0	0	0	8.42 ± 5.0	43
3	0	0	0	0	1	0	1	1	7.12 ± 3.34	51
4	0	1	0	0	0	1	1	1	5.93 ± 4.11	43
5	0	0	1	1	1	1	1	0	5.22 ± 2.74	56
5	1	0	0	0	1	1	1	1	6.20 ± 0.04	58
5	0	0	0	1	1	1	1	1	7.06 ± 0.05	67

Open eyes

2	1	0	1	0	0	0	0	0	10.86 ± 6.3	46.7
3	0	0	1	0	1	1	0	0	6.9 ± 2.9	48.9
4	1	1	0	0	0	0	1	1	6.5 ± 3	51.1
5	0	1	1	1	1	1	0	0	5.7 ± 2.8	62.2
5	1	1	1	1	0	1	0	0	5.5 ± 2.9	57.8
5	1	1	1	1	1	0	0	0	5.3 ± 2.4	71.1
7	1	1	1	1	1	1	0	1	16.7 ± 7	86.7

SC = synchrocomplex

"0" = represents EEG channels which are not functionally connected

"1" = represents EEG channels which are functionally connected

3.3. Topography of EEG functional (operational) synchrony

What are the topographic peculiarities of representative SCs presented in Tables 2 and 3?

Figures 5 and 6 illustrate representative SCs mapped onto brain schemata as connecting lines between corresponding EEG sites.

It can be seen that common SCs for closed and open eyes conditions (Fig. 5) were diverse and comprised all categories. At the same time, unique SCs specific for each condition (Fig.

6) had the following major differences: closed eyes condition was characterised by SCs with mostly fronto-central topography, whereas open eyes condition was characterised by SCs with mostly centro-parieto-occipital topography.

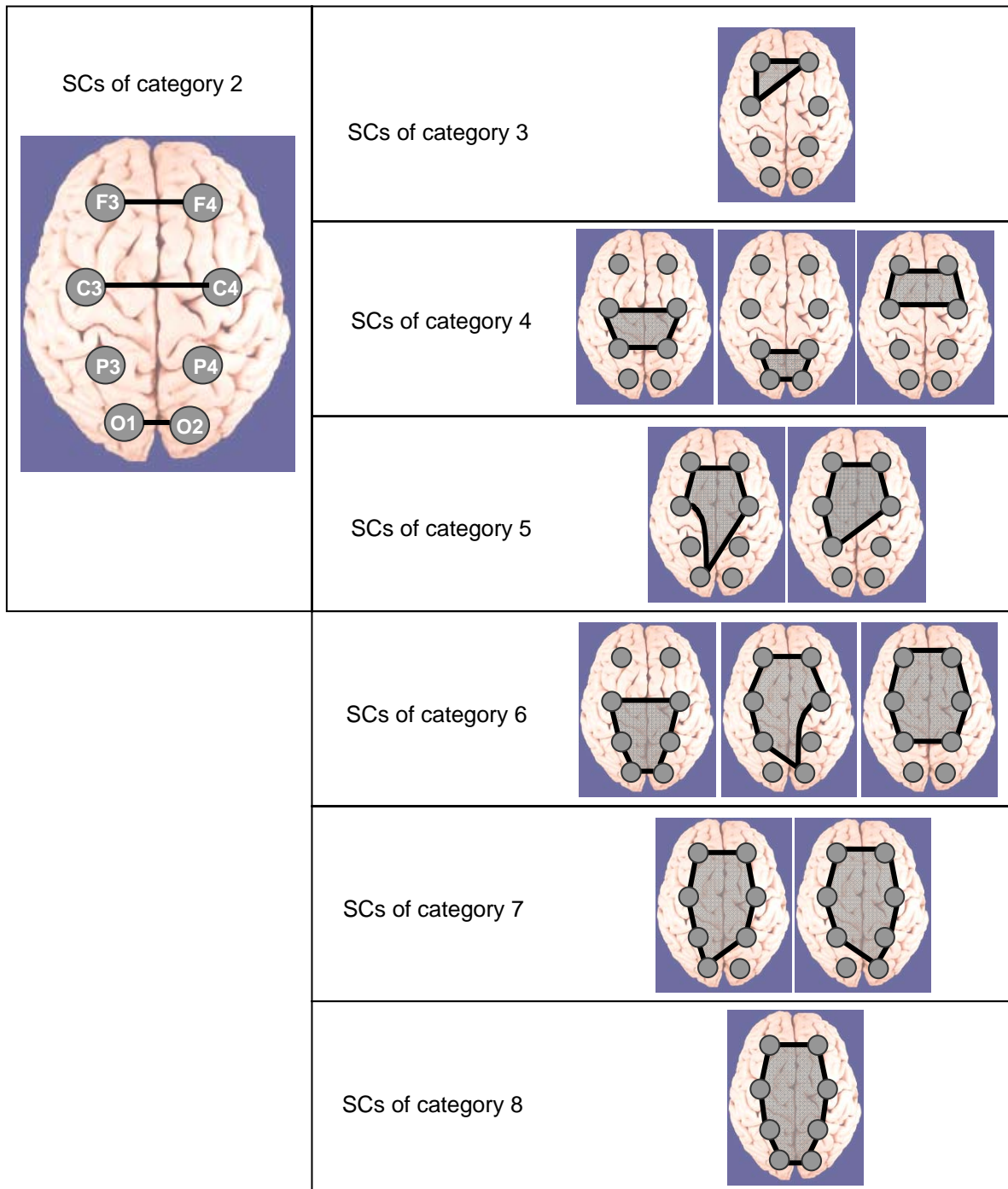
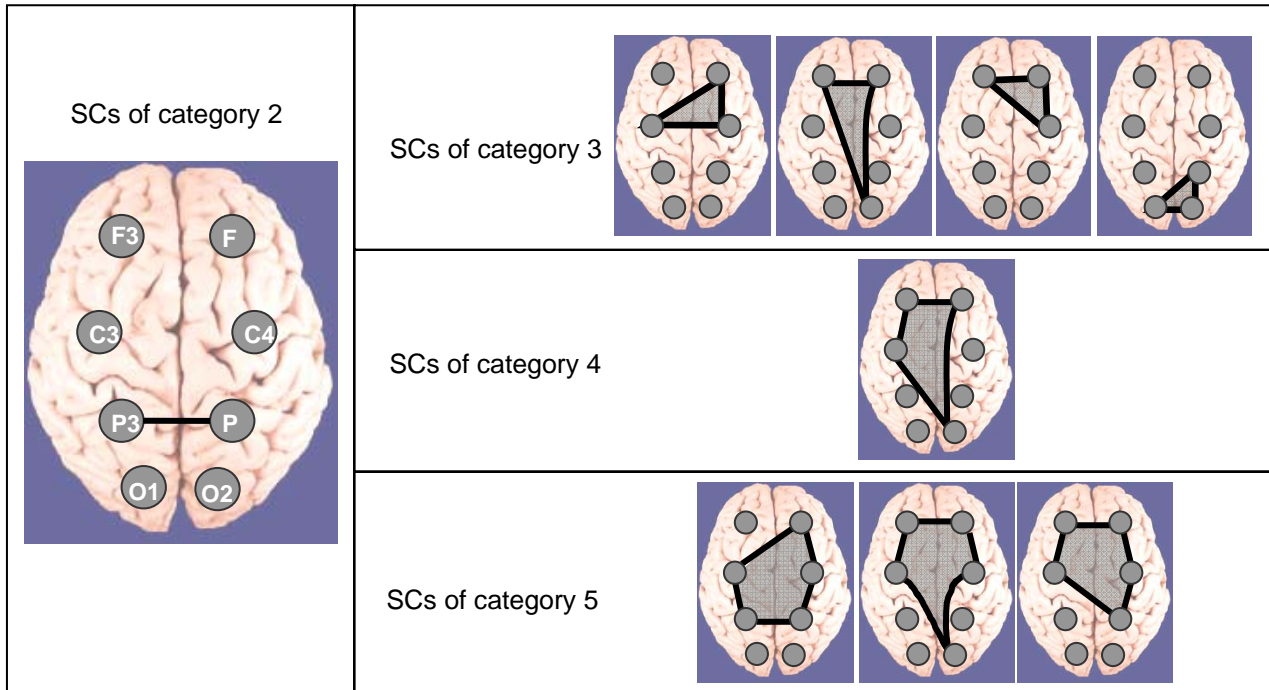


Figure 5. Common for closed and open eyes synchrocomplexes (SCs) (indexed by structural synchrony and presented at Table 1). Data averaged across all EEGs which had a given SC. The most frequent/representative SCs which occurred (a) the largest number of repetitions (in %) across all found SCs ($n = 14156$ of all SCs for closed eyes and $n = 6195$

of all SCs for open eyes) and (b) more than in 40% of EEGs are mapped onto schematic brain maps as connecting lines between the EEG channels involved. The frequency of occurrences of each displayed SC within each category is presented in the Table 1. Grey areas are used for the easier visual perception.

Unique for closed eyes synchrocomplexes



Unique for open eyes synchrocomplexes

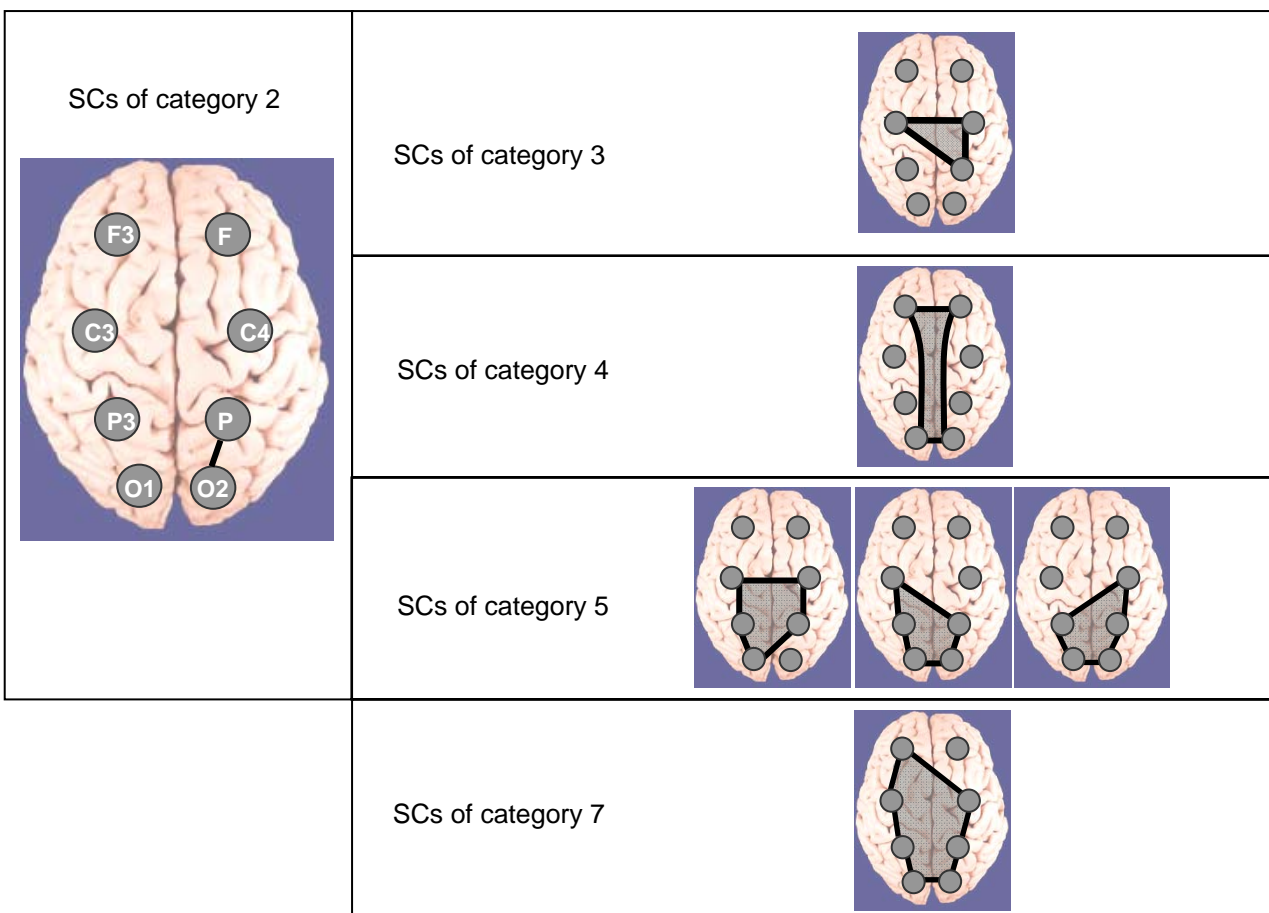


Figure 6. Unique for closed and open eyes synchronocomplexes (SCs) (indexed by structural synchrony and presented at Table 2). Data averaged across all EEGs which had a given SC. The frequency of occurrences of each displayed SC within each category is presented in the Table 2. Explanation is the same as at Fig. 5.

4. Discussion

4.1. General aspects of functional (operational) connectivity

Findings of the present study demonstrated for the first time that non-random temporal coincidence of RTPs in EEG multiple frequencies exist for both closed and open eyes conditions. This systematic between-areas synchrony of abrupt changes in EEG rhythms reflects the temporal consistency of the moments of switching between near-stationary functioning in the corresponding cortex areas. It was suggested that such switching between stationary functioning reflects a “switching” of brain operations performed by local neuronal assemblies (Fingelkurts and Fingelkurts, 2001, 2005, 2008; Kaplan et al., 2005). Systematic temporal coincidences of moments of switching between stationary functioning in different EEG channels, hence reflect a temporal coordination of brain operations performed by remote neuronal assemblies (Fingelkurts and Fingelkurts, 2001, 2005, 2008; Kaplan et al., 2005; Fingelkurts et al., 2005).

Both conditions were characterised by less operational synchrony between any 2 and 3 cortex areas and by more operational synchrony between any 6, 7 and 8 cortex areas than what is expected by chance. This means that during resting conditions small groups of cortex areas tend to work independently (by a sufficient degree of temporal dis-coordination of operations), whereas large groups of cortex areas “prefer” coordinated regime of functioning (in frequency domain).

Of course, not every case of sharp transformation in EEG frequency is an indicator of “switching” of brain operations and, correspondingly, not all cases of coincidences of RTPs give evidence of synchronization of operations. However, considering the main tenets of operational architectonics (Fingelkurts and Fingelkurts, 2001, 2004, 2005, 2006, 2008), the fact that used connectivity measure is sensitive to the morpho-functional organization of the cortex rather than to the volume conduction and/or reference electrode (for relevant details, see Kaplan et al., 2005; Fingelkurts and Fingelkurts, 2008) and observed (a) systematicity of SCs, (b) consistent differences between closed and open eyes conditions and (c) differences

from surrogate data one may expect that the presented results mainly reflect brain operations performed by local neuronal assemblies and their remote temporal coordination.

Specifically, we found that the process of synchronisation of operations (indexed by temporal coincidences of RTPs in EEG multiple frequencies between different EEG channels) performed by different neuronal assemblies was highly expressed in both resting conditions (closed and open eyes). Indeed, each EEG channel participated in more than 50% of all SCs (Fig. 4A) and intensity of this participation was above 97% (indexed by the percent of RTPs in each EEG channel which were synchronised with RTPs from other channels) (Fig. 4B). Such a pronounced synchronisation process of the changes in EEG multiple frequencies during rest is consistent with the work of Fingelkurts and co-authors (Kaplan et al., 1997; Fingelkurts, 1998) where synchronisation process of the abrupt changes in EEG amplitude was studied. A relatively high level of operational synchrony between RTPs in EEG amplitude was always present during resting state (Fingelkurts and Fingelkurts, 2010a).

In the present study the synchronisation process was expressed to a lesser extent in posterior EEG channels than in the anterior channels (Fig. 4A and B). This is in line with the work of Shishkin (1997) where the author has demonstrated a similar effect, but in the EEG amplitude domain. It can be explained that during resting conditions frontal areas are characterised by more dynamic transitions between different neuronal assemblies' operations and by more intense involvement in synchronisation process than occipital areas, probably reflecting personal identity and past personal experiences (Luria, 1973), coordination of basic drives and plans (Raichle and Gusnard, 2005) and complete self-consciousness (Uhtomskiy, 1966). It was suggested that exactly these processes are active during rest (Gusnard et al., 2001).

Both closed and open eyes conditions were characterised by a diverse variety of the most frequent SCs with different order of area recruitment (Table 2 and 3; Fig. 5 and 6). Perhaps this diversity reflects the poly-operational structure of brain activity during rest, where cortical processes are not determined by external stimuli but are driven by free floating associations, mental imagery, planning, etc. Indeed, it was demonstrated that ongoing brain activity occurs in discontinuous steps and confirms that the cerebral cortex is continuously active in wakefulness (for discussion see Fingelkurts et al., 2003b). This is in line with the works of Thatcher and John (1977), Herscovitch (1994), Arieli et al. (1996), Tsodyks et al. (1999), Raichle et al. (2001), Raichle and Snyder (2007) and others who demonstrated a

highly organized intrinsic functional activity (i.e., activity which is not directly related to identifiable sensory or motor events) during a resting state. Metabolic data confirm these studies. The resting human brain consumes 20% of the body's energy (even though it represents only 2% of total body mass), most of which is used to support ongoing neuronal activity (Ames, 2000; Attwell and Laughlin, 2001; Lennie, 2003; Shulman et al., 2004; Raichle and Mintun, 2006). At the same time, task-related increases in neuronal metabolism are usually small (<5%) in comparison with the large resting energy consumption (Raichle and Mintun, 2006).

Among all types of SCs, those that involved 4–6 cortex areas were dominant during rest conditions (closed and open eyes). Perhaps frequency domain coordinated activity of 4–6 cortex areas is optimal for resting wakefulness.

4.2. Functional (operational) connectivity during open eyes versus closed eyes

This study demonstrated that in spite of common general characteristics of the synchronisation process for both resting conditions, each of the states had its own distinguished peculiarities.

We found that eyes opening resulted in widening and intensification of synchronization process when compared with closed eyes. This was reflected in a higher percent of SC which involved 6–8 cortex areas (Fig. 3) and more intense participation of each examined cortex area in SCs (Fig. 4A and B) during open eyes when compared with closed eyes condition. Recall that synchronisation of RTPs here corresponds to the dynamic temporal coordination of shifts among brain operations performed by remote neuronal assemblies (Fingelkurts et al., 2005). It is assumed that RTPs in the EEG signal reflect the moments of switching between the elementary units of informational processing in the brain – operations (Fingelkurts and Fingelkurts, 2001, 2005, 2008). In this context, the aforementioned findings perhaps reflect more dynamic and wider information processing during open eyes condition in comparison with closed eyes. Keeping that in mind we may conclude that changes in the brain functional state were accompanied by changes in the poly-operational structure of brain activity. Indeed, as it has been shown, the eyes-open resting condition indicates an increase in non-specific activation caused by basic sensory input (Gevins et al., 1997; Klimesch, 1999; Klimesch et al., 2001) and by an orienting reaction of the brain (Jung, 1953) which reflects general task

demands and attentional processes (Sokolov, 1963; Klimesch, 1999; Pfurtscheller and Lopes da Silva, 1999; Verstraeten and Cluydts, 2002; Babiloni et al., 2004; Mantini et al., 2007).

Supposition on more intense information processing during open eyes than during closed eyes is supported also by the lesser percent of given SC types within a particular category during eyes open condition than in closed eyes condition (Table 2) found in the present study. It means that open eyes was characterised by larger number of different types of SCs and as a consequence by more dynamic shifts among them compared to those observed during closed eyes.

Additionally, we found that open eyes condition was characterised by unique SCs with mostly centro-parieto-occipital topography, whereas closed eyes condition was characterised by SCs with mostly fronto-central topography (Fig. 6). Characterisation of closed eyes condition by unique specific SCs with mostly fronto-central topography may reflect dominant involvement of networks which associated with internal processing (Mantini et al., 2007) and with the stimulus-independent thought, mind-wandering and the internal “narrative” (Gusnard et al., 2001). In contrast, characterisation of open eyes condition by specific SCs with mostly centro-parieto-occipital topology most likely reflects dominant involvement of networks which associated with focused attention and visual processing (Mantini et al., 2007). Thus, spontaneous ongoing oscillatory activity during rest depends on the dynamic interplay between distinct functional networks, each characterized by a specific electrophysiological signature (SC of particular type). It is assumed that during different behavioural and cognitive acts these resting-state-networks (indexed by SC types) would be dynamically assembled and modulated forming new specific task-related-networks.

4.3. Topographic aspects of functional (operational) connectivity

The inter-channel coordination of SP-segments enables us to characterize EEG from the viewpoint of more or less general coordination between its short-term local spectral descriptions. Notice that analysis performed in this study does not permit to make any inferences on primary generators (sources) of the EEG activity.

Observed diversity of spatial SP-maps (Figs. 5 and 6) demonstrated that the dynamics of topographic variability of short-term SP-segments appear to reflect the piecewise stationary process of functional integration of cortex areas. It is suggested that brain activity during

resting wakefulness is topographically organized in discrete brain networks – resting state networks (Mantini et al., 2007) which functionally shift each other. It is likely that the pattern of the functional stabilization of the cortical inter-area relations can be expressed as a mosaic of dynamic constellations of different operations executed by remote brain regions – “operational modules” (Nunez, 1989; Fingelkurts and Fingelkurts, 2001, 2004, 2005, 2008). The lifetime of such spatial operational modules is determined by the duration of the period of joint stabilization of the main dynamic parameters of the activity of neuronal assemblies which are involved in these modules. At the level of EEG, this process is reflected in stabilization of the SPs-segments in corresponding EEG channels that comprises a metastable state (Fingelkurts and Fingelkurts, 2004, 2008; Werner, 2007). As has been proposed by Kelso (1995) metastability relates to the phenomenon of a constant interplay between the autonomous and interdependent tendencies in the system’s (in our case a brain) dynamics (see also Bressler and Kelso, 2001). In this context each operational module is a metastable spatial-temporal pattern of brain activity because the neuronal assemblies which constitute it have different operations/functions and do their own inherent tasks (thus expressing the autonomous tendency), while still, at the same time, being temporally entangled among each other (and thus expressing the coordinated activity) in order to execute a common complex operation or complex cognitive act of a higher hierarchy (Fingelkurts and Fingelkurts, 2004, 2005; Fingelkurts et al., 2009).

In this context the participation of cortex areas in the organization of a common functional act is reflected not so much in the presence of a shared EEG rhythm in different EEG channels (distant neuronal ensembles), but in the systematic coincidences of the moments of switching between EEG frequency modes in the cortex areas. It seems that cortical networks can display different states of coordination independently of their correlation and coherence, using shifts in brain oscillations at multiple frequencies based on the size and configuration of the neuronal assemblies involved (Lopes da Silva, 1991).

4.4. Comparison with surrogate data

All results of the present study would be difficult to interpret without comparing them with similar data obtained for EEG with artificially created complete temporal mismatch of SP-segments between all 8 EEG channels. The study demonstrated that random combination of RTPs of SP-segments “creates” totally different estimates of spatial-temporal stabilization of

SP-segments than is observed under conditions when the EEG channels are functionally correlated (Figs. 3 and 4). The results of the surrogate tests for statistical validity indicated that our findings are indeed caused by coordinated changes of the oscillatory states in the EEG and cannot be explained by mere random processes.

Before coming to the final conclusions, a technical question should be raised: whether the reported cortical spatio-temporal modules, within which steady relations are formed by the mutual stabilization between the types of SP-segments in each EEG channel are real or are affected by the volume conduction between electrodes? The effect of volume conduction on presented results is unlikely because (a) Functional connectivity measure used in this study is free from EEG signal similarities between different EEG channels and, thus free from direct influences of volume conduction because it is the similarity of EEG signals on the scalp that is determined to a large degree by volume conduction; (b) Connectivity measure used in this study is based on temporal point-to-point coincidences of RTPs (even for remote cortex areas), but spreading of electrical activity by volume conduction takes some time especially for remote areas. Therefore, whenever synchronisation between cortical areas has time-lag = 0 ms then functional connectivity measure does not reflect volume conduction; (c) It was demonstrated earlier that connectivity measure based on temporal coincidences of RTPs is sensitive to the morpho-functional organization of the cortex rather than to the volume conduction and/or reference electrode (for relevant details, see Kaplan et al., 2005; Fingelkurts and Fingelkurts, 2008, 2010b); (d) If presented results would be determined mostly by volume conduction, then surrogate data (where the natural time relations between EEG channels were completely destroyed) would not show systematic differences from the actual EEG. This however was not the case (see Fig. 3 and 4); (e) Converging evidences indicated that EEG synchronization observed for electrodes separated by 4 cm or more is not spurious (for discussion see Ward and Doesburg, 2009). In current study it is the case as only 8 electrodes were used; (f) The accuracy of topographic EEG mapping for determining local (immediately under the recording electrode) brain activity was already established by Cook et al. (1998) (see also Bullock, 1997; Kaiser, 2000; Freeman, 2003); (g) The skin and skull are not considered to be serious frequency filters (Nunez, 1995) and (h) It has been shown that EEG and MEG (which is free from volume-conduction effects) offer comparable spatial resolutions on the order of several millimetres (Cohen et al., 1990; Ingber, 1991). Dipole localization accuracy of 7–8 mm for EEG and 3 mm for MEG has been demonstrated using a

human skull phantom (Leahy et al., 1998). Thus, spatial resolution of an EEG might be better than widely believed.

Additionally, the presented results cannot be attributed to the EEG recording with linked ear reference electrode or volume conduction for the following reasons: (a) The spatial synchrony could not be attributed to referential recording, because an event occurring at the reference electrode would appear to be the same on all channels and between actual and surrogate EEGs, whereas the number of RTPs varied across the channels and differed significantly between actual and surrogate EEGs; (b) amplitude in the delta, theta, alpha, and beta bands did not vary significantly as a function of reference (Ferree et al., 2001); (c) the occipital and frontal regions clearly showed different accentuations in their EEG effects and (b) our analysis revealed the existence of high diversity of SCs and high number of asymmetric SCs. Thus, taken together these arguments we may conclude that reported results in this study are virtually unaffected by volume conduction and chosen reference electrode.

Concluding remarks

Taken together, the results of this study demonstrated for the first time the existence of non-random temporally coordinated patterns of switching (on/off) moments in EEG rhythms. Such synchrony in EEG frequency domain was observed independently from functional state of the brain (closed eyes *vs* open eyes conditions). However, topographic extent and the intensity of the synchrony in EEG frequency domain were functionally dependent: different for closed and open eyes. It was suggested that changes in the brain functional state during rest were accompanied by changes in the poly-operational structure of brain activity (indexed by temporally coordinated changes in EEG SPs description) (for discussion see Fingelkurts et al., 2003b).

The fact that observed results were significantly different from surrogate data reflects a non-occasional/non-random nature of spatio-temporal organization of EEG in the frequency domain. Thus, the process of operational synchrony in EEG frequency domain is not an epiphenomenon of brain activity.

Analysis of topographic SP-segments variability may permit researches to trace episodes of the metastable cortical inter-area cooperations independently on partial correlation and/or coherency between the local EEGs.

Considering that principles of operational synchrony were demonstrated for EEG frequency domain (present study), for EEG amplitude domain (Fingelkurts and Fingelkurts, 2001, 2005, 2006, 2008, 2010a) and to some extent for EEG phase domain (Freeman and Rogers, 2002; Freeman and Holmes, 2005; Kozma et al., 2005) it is reasonable to suggest that operational synchrony is a universal phenomenon for different dimensions of electromagnetic brain field in which complex brain functioning is reflected.

Further studies should extend presented analysis to a larger number of EEG channels and to broader frequency band including gamma frequency range to capture more detail picture of operational synchrony.

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Conflict of interest statement

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Appendix

A probability-classification analysis of the short-term EEG SPs

The general idea of probability-classification analysis is that sequential single EEG SPs are classified within each channel of 1-min EEG using a set of standard SPs.

Probability-classification analysis of the short-term EEG SPs was performed at several steps.

During the first step, standard SPs were generated from the data itself (not before-hand). The set of standard SPs was formed automatically using heuristic procedures and Pearson's correlation coefficients (CC): A pool of SPs ($n = 157,224$) was built from all the SPs of the entire EEG signals (all locations) for all subjects and both conditions. From this pool, all identical SPs with dominant power peaks (peaks that rise significantly above the general average) were counted automatically. The peak detection was based on normalizing the SP to within-SP relative percentages of magnitude, where acceptance is achieved when the peak exceeds a given (60%) percent-magnitude (100% corresponds to the magnitude of the highest peak within the SP). According to the preliminary study, this value has proved to be the most effective for peak detection.

The set of SPs with the highest count were the most probable candidates to form the "set of standard SPs." Only those SPs with a minimum mutual correlation were selected. As a result, the standard set included 26 SPs in this study (Fig. 7).

The main frequency peaks for each SP class are: 1 - 2.5 Hz, 2 - 4 Hz, 3 - 5.5 Hz, 4 - 7 Hz, 5 - 10 Hz, 6 - 11.5 Hz, 7 - 13 Hz, 8 - 2.5-4 Hz, 9 - 2.5-5.5 Hz, 10 - 3-6.5 Hz, 11 - 2.5-8.5 Hz, 12 - 2.5-10.5 Hz, 13 - 2.5-12.5 Hz, 14 - 4-8.5 Hz, 15 - 4-10.5 Hz, 16 - 5.5-10.5 Hz, 17 - 6.5-12.5 Hz, 18 - 8.5-11.5 Hz, 19 - 9.5-10.5 Hz, 20 - 9.5-11.5 Hz, 21 - 2.5-4.5-8.5 Hz, 22 - 2.5-4.5-10.5 Hz, 23 - 3-6.5-11 Hz, 24 - 2.5-3.5-5.5-9.5 Hz, 25 - 2-6.5-8.5-12.5 Hz, 26 – polyrhythmic SPs (the category of unique SPs which is comprised of SPs which reflect transitory and/or noisy/disorganised episodes in the EEG).

Notice that there is no universal set of standard SPs: different EEG data (different study) requires formation of new set of standard SPs. According to our experience the sets of standard SPs from different studies overlap significantly, but they are not identical neither in number of SPs, nor in SP's types.

During the second step, the initial matrix of cross-correlations between standard and current individual SPs of analyzed EEG was calculated for each channel separately (Fig 8). The current SPs that their CC passed the acceptance criteria of $r \geq 0.71$ were attributed to their respective standard classes. Therefore, the same current SPs may be included simultaneously

into different standard classes. The *CC* acceptance criteria r was determined such as for $r \geq 0.71$ more than 50% of the SP variances were coupled/associated.

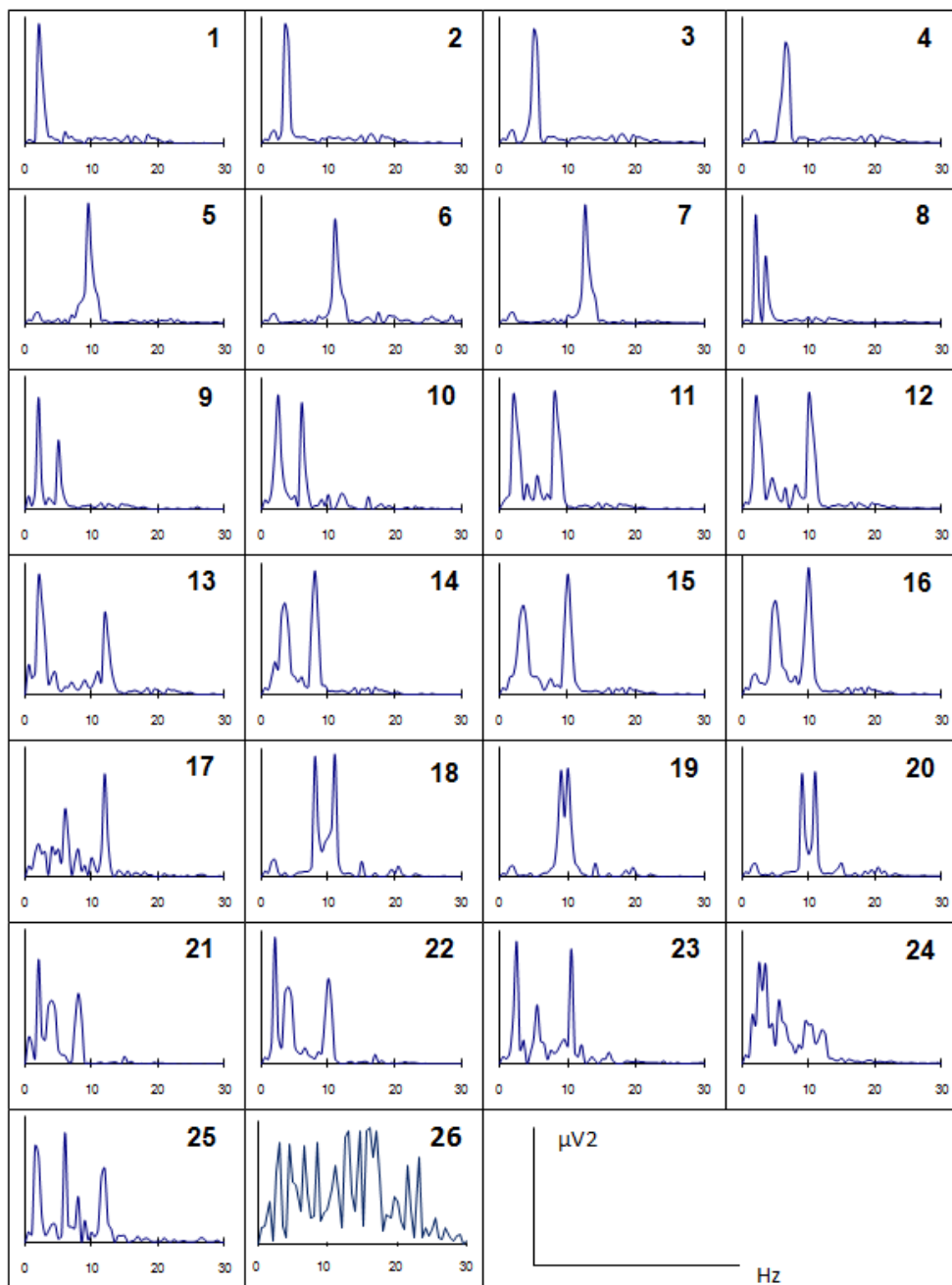


Figure 7. A set of standard SPs which was found automatically for a given EEG data.

The main frequency peaks for each SP class are: 1 - 2.5 Hz, 2 - 4 Hz, 3 - 5.5 Hz, 4 - 7 Hz, 5 - 10 Hz, 6 - 11.5 Hz, 7 - 13 Hz, 8 - 2.5-4 Hz, 9 - 2.5-5.5 Hz, 10 - 3-6.5 Hz, 11 - 2.5-8.5 Hz, 12 - 2.5-10.5 Hz, 13 - 2.5-12.5 Hz, 14 - 4-8.5 Hz, 15 - 4-10.5 Hz, 16 - 5.5-10.5 Hz, 17 - 6.5-12.5 Hz, 18 - 8.5-11.5 Hz, 19 - 9.5-10.5 Hz, 20 - 9.5-11.5 Hz, 21 - 2.5-4.5-8.5 Hz, 22 - 2.5-4.5-10.5 Hz, 23 - 3-6.5-11 Hz, 24 - 2.5-3.5-5.5-9.5 Hz, 25 - 2-6.5-8.5-12.5 Hz, 26 - polyrhythmic SPs.

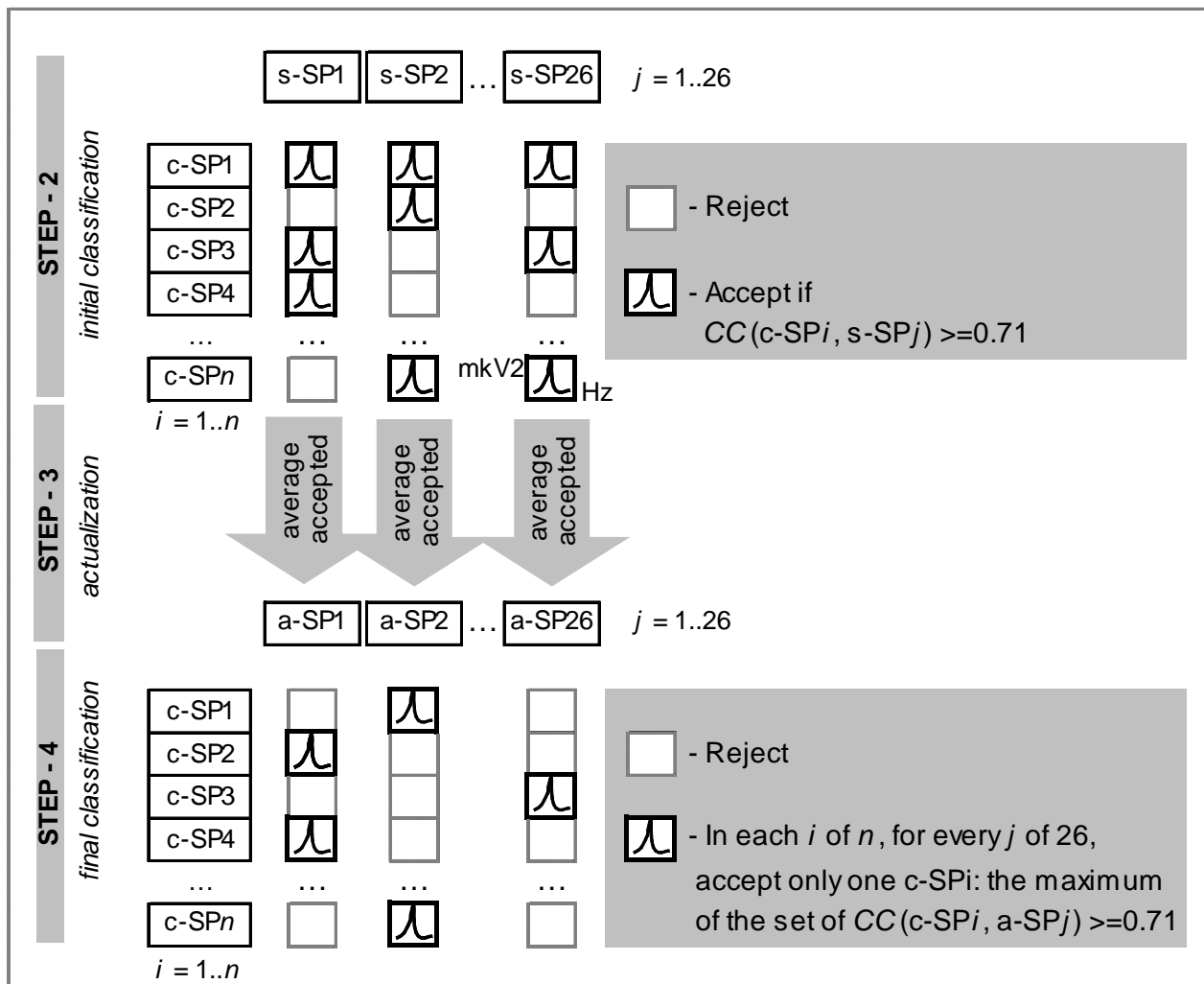


Figure 8. Second, third and fourth steps of a probability-classification analysis of the short-term EEG SPs.

s-SP_j – standard spectral pattern of type j , c-SP_i – current spectral pattern of type i , a-SP_j – actual spectral patterns of type j , CC – coefficient of correlation.

During the third step, the current SPs included in a particular class were averaged within this class (Fig. 8). The same procedure was performed for all classes separately for each EEG channel. On the back of this, the standard spectra were reconstructed but this time taking into account the peculiarities of the spectral description of concrete channel of the particular EEG. In this way an “actualization” of the initial standard SP set was performed. In other words, standard SPs were converted into so-called actual spectral patterns. Notice that the main frequency peaks in the *actual* SP of every class stay the same as in the corresponding *standard* SP’s classes. However, overall shape of the power spectrum was automatically

modulated in the direction to better represent the multitude of all SPs within each class in a given EEG channel.

An actual SP set was in turn used for the fourth step – the final classification of the current SPs: each of current SPs was attributed to only one actual SP class for which the *CC* was the *maximum* of the set of $r \geq 0.71$ (Fig. 8).

The probability-classification technique employs two correction algorithms to achieve a significant reduction in the variance of single spectral estimations and to take into account the relationship between neighbour frequencies in the frequency continuum (Kaplan et al., 1999; Fingelkurts et al., 2003a): (a) spectrum glide smoothing, (b) choosing the maximum *CC* out of the three values of the correlation function, which was calculated between the standard SP and the current SP on zero shift and on double-side shift by one step (± 0.5 Hz). According to tests and modelling calculations, the latter procedure was chosen in this study. This justifies the use of individual short-term SPs and increases the sensitivity of this analytical approach in revealing the dynamics of EEG oscillatory patterns. This SP classification method made it possible to identify up to 100% of the individual single spectra in the EEGs due to the algorithm's ability to adapt to local signals. Therefore at every time step a valid classification was reached, i.e., there was no 'undecided' category.

Considering that a single EEG spectrum illustrates the particular integral dynamics of tens and hundreds of thousands of neurons in a given cortical area at a particular point in time (Dumermuth and Molinari, 1987), it can be said that the SPs within each class are generated by the same or similar dynamics with the same or similar driving force. SPs from different classes, however, have had in effect different driving forces and therefore have been generated by different dynamics (Manuca and Savit, 1996). In this case, one type of SP may be considered as a single event in EEG phenomenology from the viewpoint of its spectral characteristics (Fingelkurts and Fingelkurts, 2010b). In this context, this analytical approach implicitly considers the non-stationarity of EEG (for the review on EEG non-stationarity see Kaplan et al., 2005).

As a result of the probability-classification technique, each current SP was labelled according to the index of the class to which it belongs. Thus, a sequence of SP labels that represents the sequence of EEG oscillatory states through which the system passes was obtained. Hence, each EEG signal was reduced to a sequence of individually classified SPs (Fig. 1).

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