

Correlation of EEG Envelopes is the Best Method for Identifying Mental Diseases, Functional States, Individual and Intergroup Differences

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Received: 12 June 2021 Accepted: 1 July 2021 Published: 15 July 2021

Abstract

The principal errors of spectral and coherent analysis are discussed, and the mathematics of these methods is not related to EEG nature. In this regard, in 2011, the new method was developed for evaluating EEG synchrony by the correlation of envelopes, which has a direct and fundamental physiological meaning. The basics of this method and the methodology of subsequent multilateral statistical analysis are considered. The effective use of the method for identifying individual and intergroup differences in the norm and several types of schizophrenia, depressive diseases, five stages of sleep, and similar functional states are presented.

Index terms— EEG, metrology, amplitude and power spectra, coherency, envelope, correlation.

1 Introduction

Unfortunately, in the field of computational or quantitative EEG (qEEG), metrological criteria, assessments and standards have not been formed globally for several of reasons [1]. As evidenced by the content of the special fundamental monograph [2] and many journal publications on qEEG, metrological issues almost do not attract the attention of EEG researchers. The new proposed mathematical methods are not compared with analogs; their effectiveness in solving typical physiological problems is not evaluated, is not compared and is not statistically verified. Traditional methods are not critically examined and rethought. Periodically, attempts are made to introduce completely exotic and unrelated brain physiology methods from the theories of chaos, information, and entropy, fractals, attractors, automatic regulation, nonlinear dynamics, wavelets, etc.

One way or another, but scientific research of EEG mainly followed in the wake of physical and technical applications of mathematical methods of signal analysis which were often directly and uncritically transferred by involved engineering and physical specialists without due consideration of a) the fundamental non-stationarity of biosignals; b) the inharmonic nature of their sources; c) the presence of Author: Lomonosov Moscow State University, Biology Department, Russian Federation. e-mail: akula-@mail.ru amplitude modulation. Indeed, there is not a single wellknown a pure or applied mathematician who has contributed to the development of special methods of EEG analysis. As a result, many methods that were inadequate in this field were transferred, which, in the absence of metrological criticism, leads to incompatibility and inconsistency of the results and conclusions obtained by different researchers. And such a situation can in no way be recognized as the scientific one.

It is no exaggeration to say that the main means of qEEG are [2] spectral estimates of EEG amplitude in frequency domains and estimates of synchrony between pairs of derivations using the coherence function.

2 II.

3 EEG Amplitude Estimates

During the pre-computer era, EEG amplitude was estimated by direct measurements (DM) of EEG waves. After the FFT algorithm appearance in 1965, EEG amplitude was indirectly estimated (IdE) from the amplitude and

43 power spectra. There is no doubt that DM acts as an indisputable standard, and IdM may differ from them in
44 the resulting values. The corresponding comparison was carried out in the special metrological study [3], and it
45 showed the following differences:

46 1) The three studied in [3] 6) The largest errors were found for the power spectrum. These conclusions do not
47 allow metrologically qualify IdE as the analytical tools adequate to the nature and specifics of EEG potentials.
48 Their use may lead to the incompatibility of results obtained by different researchers.

49 In addition, the spectra have an extremely distant relation to EEG nature since, unlike sound and
50 electromagnetic signals, EEG is not the sum of harmonics. EEG is the sum of postsynaptic potentials under
51 the electrode whose short-time changes take the form of asymmetric bell-shaped functions. Therefore, individual
52 spectral harmonics have no physiological meaning. They change arbitrarily both when the length of the analysis
53 epoch changes, as well as on neighboring epochs.

54 4 III.

55 5 Coherence

56 The poorly known history of EEG coherence is a vivid example of the mass spread of pseudoscientific
57 misconception. The coherence function was formulated in 1930 by Norbert Wiener [4], implementing the idea
58 previously expressed by David Hilbert that it would be good to have something similar to Pearson correlation in
59 the spectral region. Wiener intended this function for problems of quantum mechanics and nonlinear optics,
60 which are obviously extremely far from EEG studies. Subsequently, coherence became widespread in the
61 analysis of physical signals but as a purely auxiliary indicator for assessing the significance of other crossspectral
62 characteristics [5].

63 Many years have passed when in 1963, the newly minted young Ph.D. [6], without any reference to sources
64 and predecessors, proposed coherence as the main indicator of EEG synchrony. This Ph.D. published 2-3 more
65 articles on this topic, after which he lost interest in it. But the growing snowball of coherency rolled around the
66 world, capturing the minds of many thousands of followers like a mass pandemic.

67 The special metrological analysis of the weaknesses and errors of coherence was carried out in the study [7],
68 which gave the following results:

69 1) The coherence mainly evaluates the degree of phase instability of the cross-spectrum of two EEG signals,
70 which to an even greater extent than spectral harmonics has no physiological meaning; 2) At the same time,
71 the coherence also changes depending on the ratio of the values of the crossspectrum vectors at neighboring
72 epochs 1 1 As the difference in values of vectors increases, the coherence increases, which is directly opposite
73 to the Pearson correlation , and such a dual sensitivity is unacceptable for a measuring instrument; 3) The
74 coherence dependence on phase instability has a highly nonlinear snake-like character, which is unacceptable for
75 accurate measurements; 4) The coherence values are strongly influenced by choice of four setting parameters
76 which is also unacceptable for a measuring instrument; 5) Different EEG analyzers secretly use different settings
77 of these parameters, so the obtained coherence values are incompatible. Thus, coherence evaluates unknown what,
78 unknown how, and unknown why, being an example of pseudoscientific anachronism. As the literature reviews,
79 performed in the three main areas of scientific and medical research, show [9][10][11], the use of coherence leads
80 to a total incompatibility of results on the localization of inter-individual and intergroup differences. Thus these
81 numerous publications do not belong to the field of science, which is designed to search for and finds objective
82 laws in natural phenomena, but to the category of random noise or pseudoscientific garbage.

83 IV.

84 6 Correlation of EEG Envelopes

85 In connection with the numerous and fundamental errors of coherence considered, another and adequate
86 assessment of EEG synchrony was proposed in 2011 [8] by calculating the Pearson correlation coefficient
87 between the envelopes of two EEG derivations. Unlike coherence, this assessment has a direct and fundamental
88 physiological meaning. Indeed, since the envelope represents a change in EEG amplitude modulation (fig. ??) 2
89 , it increases with increasing synchrony in the change of postsynaptic potentials under the electrode. Therefore,
90 the envelopes correlation evaluates the degree of synchrony in the dynamics of postsynaptic synchrony between
91 two EEG derivations.

92 property. Thus, Wiener, in his algorithm, distorted Hilbert's original idea. 2 Mathematically, the envelope
93 is a module of an analytical (complexvalued) signal, the real part of which is equal to the signal itself, and the
94 imaginary part is obtained from the signal by the Hilbert transform. In turn, Hilbert transform is equivalent to
95 the double Fourier transform, when before the reverse transformation, all spectral harmonics are shifted in phase
96 by 90°. A It was found that in more than 42% of cases, there are high correlations between the envelopes of
97 closely located (neighboring) derivations from 0.6 to 0.99 at the median = 0.42, while for more distant derivations,
98 98.5% of the envelope correlations do not exceed 0.6 at the median = 0.17. At the same time, highly correlated
99 connections between the envelopes form distinct topographic patterns on the scalp, which are largely preserved
100 in neighboring EEG frequency domains.

101 This allows us to reduce the amount of significant information, limiting ourselves only to the grid of connections
102 between nearby pairs of derivations; for the 10-20% scheme, such pairs will be 43 (Fig. 2, a). The use of such

103 a standard grid, in particular, contributes to the comparability of the results obtained by different researchers.
104 Within the framework of such a grid, it is easy to visualize highly correlated connections between envelopes (Fig.
105 2, a-c The sequence of correlation coefficients between EEG envelopes for pairs of derivations in their ordered
106 sequence in such a standard grid is called the profile of synchrony (PS) of the subject. It is convenient to depict
107 PS in the form of a bar chart (Fig. 2, d), which provides the researcher with an additional visual pattern. It is
108 precisely such profiles that are the source material for the further areas of analysis.

109 In the case of a group of subjects, we will have a PS matrix (Fig. ??): columns are pairs of derivations from
110 the standard grid, rows are the subjects. Such matrices can be obtained: 1) for different time intervals of the
111 same functional state; 2) for different functional states; 3) for different frequency ranges; 4) for different groups
112 of subjects that differ in certain characteristics, etc. And such matrices in further directions of analysis can be
113 compared in pairs (Fig. ??): 1) by the same pairs of derivations (by columns); 2) by the same subjects (by rows);
114 3) for all subjects, each with each; 4) for pairs of derivations each with each.

115 Fig. ??: The example of two matrices with profiles of synchrony for two groups of subjects and three variants
116 of its comparison.

117 V.

118 7 Methodology of the Subsequent Analysis

119 After calculating PS of two or more groups of subjects, it is necessary to identify and reliably statistically
120 justify the existence of differences of interest to the researcher [8]. For individual pairwise comparisons, there
121 are several options (Fig. ??). The similarity of the compared pairs is estimated by the correlation coefficients
122 of Pearson, Spearman, Kendell, etc., and the differences are estimated by the parametric and nonparametric
123 criteria of Student, Fisher, Wilcoxon, signs, Ansari Bradley, Klotz, Kolmogorov-Smirnov, etc. Thus, it is possible
124 to identify completely different PS patterns characteristic of pathology and norm groups (Fig. 4). Simultaneously,
125 it should be remembered that with several paired comparisons at the same time, it is necessary to adjust the
126 critical level of significance of null hypotheses using the Bonferroni correction. Further, it is possible to study
127 the difference and similarity of PS of each subject in different frequency domains and at different time intervals
128 to assess the stability of the functional state. Here, according to the correlation coefficients r_{jj} between PS of
129 each j -th subject in two adjacent frequency domains or on neighboring time intervals (Fig. ??), it is possible to
130 make inter-individual comparisons and ranking of the subjects.

131 The next direction is the use of multidimensional statistical methods to identify intergroup differences. The
132 differences of the matrices in the average PS values are estimated using the 2-ways ANOVA method.

133 The next step may be to use factor analysis for each matrix to identify PS, mainly projected on the principal
134 factor axes. As follows from Fig. 5, these projections are fundamentally different for the norm and pathology
135 groups. To quantify the differences, it is possible to calculate correlations between the factor loadings of PS for
136 each factor performed between the two groups of subjects. As a result, the correlations for the three principal
137 factors are obtained at a minimum of 0.106-0.328, which indicates a fundamental difference in factor structures
138 and intergroup differences. One of the most important methods is to use the discriminant analysis, which allows
139 us to construct a classifying function for a statistically reliable and stable division of subjects into two analyzed
140 groups. Such a function can be practically used to assign new individuals to a particular group, that is, as a
141 means of preliminary medical or functional diagnostics.

142 8 VI. Identification of Highly Consistency Groups of Subjects

143 One of the important statistical tasks is the identification and processing of outliers and the selection of
144 homogeneous groups of subjects, which, unfortunately, are almost not taken into account in EEG studies. Such
145 outliers are the result of the action of extraneous and accidental causes that can mask really existing patterns.
146 Inattention to these issues may lead to the identification of pseudo-significant or pseudo-notsignificant individual
147 and intergroup differences.

148 Since in the method under consideration, we do not have samples of variable values, but PS are the sets of
149 measurements, so we do not apply the usual method of detecting outliers by large deviations from the average
150 value. Therefore, a special method of averaged correlations of PS was developed [8]. In this case, for each group,
151 paired correlations r_{jk} between PS of all j, k -subjects are calculated at given time interval. Then we get a square
152 correlation matrix $|r_{jk}|$ by which the average value $M_j(r_{jk})$ from its correlation with all other k th subjects
153 is determined for each j -th subject. Then, using the obtained $M_j(r_{jk})$, variation series or Quetelet graphs are
154 constructed (Fig. 6), on which subjects with low consistency or outliers are distinguished. They may be the result
155 of uncontrolled features of current functional and mental state or errors in diagnosis. Therefore, they should be
156 removed from further analysis. Fig. 6 also shows a higher value of average consistency in pathology group M_j
157 $(r_{jk})=0.505\pm 0.12$ in comparison with norm group $M_j(r_{jk})=0.397\pm 0.084$ with their significant difference at
158 the significance level $p<0.00005$. This confirms a well-known rule: «every healthy person is healthy in his own
159 way, but all the "sick" persons are sick in the same way». This is a real confirmation of the effectiveness and
160 adequacy of the envelope correlations method.

9 VII. Results of the Method Application

The described method of envelope correlations (MEC) was used to assess various mental diseases and functional states. EEG recordings were carried out in a state of relaxation with closed eyes according to 10-20% system of derivations.

The material included adolescents aged 10-14 years: 39 schoolchildren without mental disorders (the control or norm group) and 45 patients with schizophrenic disorders in categories F20, F21, F25 according to ICD-10.

The following significant results were obtained: 1) numerous topographic patterns that are far from a random distribution (Fig. 2, 5); 2) proximity of topographic patterns in neighboring frequency ranges (Fig. ??, 8); 3) higher stability of functional state over time in the norm group; 4) higher interindividual consistency of pathology group (Fig. 6); 5) difference of pairs of derivations with high synchrony in the two groups of subjects (Fig. 8); 6) higher synchrony in the norm group (Fig. ??); 7) a consistent decrease in synchrony from the frontal interhemispheric connections to the occipital ones in both groups (Fig. ??); 8) a difference in topography of hemispheric dominance with its wider spatial representation in pathology group (Fig. 8); 9) a strong factor structure of PS in both groups with the predominance of four main factors; 10) a qualitative and quantitative difference in the factors acting in two groups (Fig. 5).

Further, the MEC results were compared with five other well-known synchrony estimates in the literature: coherence [7], inter-segment synchrony [12], correlations between the frequency parts of amplitude and phase spectra [13] and between filtered EEG. a) Schizophrenia [8] According to the indicators of descriptive statistics, MEC differed favorably from other methods in terms of centering and uniformity of its values distribution in 0-1 region.

The discriminant classification gave the best results in ?, ?, ?1 domains with 2-3% errors for each group compared to 5.5-28.2% errors when using other methods [14][15][16][17]. Statistical modeling showed that the resulting small percentage of MEC errors differs significantly from the random one at the significance level $p < 0.005$. Then, EEG measurements of amplitudes in derivations were added to the PS matrices, which led to 100% reliable, error-free classification.

To substantiate the practical significance of the results obtained, a control check was carried out. To do this, the pathology group was randomly divided into two ones in a ratio of 3:2 -the learning and classified samples. The discriminating function was calculated from learning sample, which was then used to assign to a particular group of classified subjects. Using of ? domain and consistent subgroups of subjects gave the best result: 1.5% of errors in learning classification and 6.2% of errors in control classification. It should be noted that such important control checks have never been carried out anywhere and by anyone.

The material included three groups of 8-15 years adolescents: 36 schoolboys without mental disorders (the norm N group), the group of 45 patients with the diagnosis of F20 schizophrenia, and the group of 80 patients with the diagnosis of F21 schizotypal disorder. Fig. ??: Differences in interhemispheric synchrony for five frequency domains ($\tau = 0.04 \pm 0.0004$). The values averaged for each group, synchrony (vertical axes) are shown for derivation pairs: F3-F4, C3-C4, P3-P4, O1-O2 (horizontal axes). Group markers: circles -F20, squares -F21, triangles -N. Below graphics, the designation of reliable intergroup differences is shown in number notation: 1 -F20-F21, 2 -F20-N, 3 -F21-N. b) Schizophrenia [9] The results of the performed complex analysis reveal the complicated picture of regional, interhemispheric differences in EEG synchrony between two schizophrenic disorders and the norm. In particular, most of the patterns listed at the beginning of Section VIIa were confirmed. It is necessary to emphasize, that in this study not only the usual problem of differentiation of norm and pathology was considered, but at the same time also the non-depicted earlier in literature more complex task of detection of subtle differences between the two close nosologies. The significant differences between F20 and F21 groups appear mainly in frontal and occipital areas in certain frequency domains. Besides, in occiput, interhemispheric and intrahemispheric synchrony for schizophrenia (F20) in some cases was closer to normal. In contrast, for schizotypal disorder (F21), intrahemispheric synchrony is higher than normal, but interhemispheric synchrony is below than normal. Certain relationships of this kind are also observed in parietal, temporal, and central areas.

One the distinctive and stable component of mental disorders in comparison with the norm is the presence of the vast areas of low synchrony separating isolated frontal and occipital intrahemispheric areas with synchrony near to normal level (Fig. 8). The presence of such a reduction and detection of right-sided asymmetry can indicate a substantial violations of interhemispheric and frontal-occipital relationships for the schizophrenic and schizotypal disorder, which fits into the framework of the well-known theory of disintegration of cortical electrical activity.

The intergroup comparison reveals the crosswise area of the sharp decrease in synchrony of pathology groups ("downfall") in comparison with the norm, including sagittal-interhemispheric and axialcentral segments (Fig. 8). It's possible that this indicates significant violations of interhemispheric and frontooccipital relationships at disorders of the schizophrenic spectrum. When comparing of two pathology groups (F20-F21), in many frequency domains we also observe distinctive regional and interhemispheric areas of increase-decrease of synchrony.

Four psychometric tests were performed on all patients: volume of direct reproduction defined by the technique of memorization of 10 words under verbal presentation; volumes of simple and difficult paired associates; runtime of Schulte tables execution. Indeed, violation of cognitive functions is one of the main consequences of schizophrenia. Several high correlations between psychometric indicators and local estimates of synchrony for each of F20 and F21 groups were revealed.

224 The main results of discriminant classification are the following: 1) δ domain provides the lowest percentage of
225 classification errors; 2) θ domain is the next one by its discriminant sensitivity; 3) association of PS of these two
226 frequency domains gives the exact classification of three groups without any The obtained results favorably differ
227 from several of alternative approaches using other indicators and more also be emphasized, that the efficiency
228 for classification of δ domain was also found in the previous study.

229 Numerous confirmations of the results of the previous study in different groups of patients indicate the stability
230 and effectiveness of MEC compared to the above-mentioned randomness of the coherent analysis results.

231 The material included two groups of older adults aged 49-82 years: 1) 11 men and 40 women with
232 the psychogenically provoked depressive reaction of bereavement: category F43.21 according to ICD-10,
233 HDRS= 22 ± 5.09 on Hamilton scale; 2) a control group of 18 men and 11 women without depressive disorders.

234 The results of the analysis revealed a complex picture of regional and interhemispheric differences in EEG
235 synchrony between the norm and depressive deviations, including different ratios of greater?less or the same
236 synchrony in activity of different cortical zones. One of the principal features of the obtained integral picture is the
237 presence of extended zones of sharply reduced synchrony of neurophysiological activation processes in depression,
238 covering the entire premedial region in the forehead-occipital direction, including interhemispheric connections,
239 as well as lateral frontotemporal connections in both hemispheres. In the same time, a single topographic picture
240 of changes in EEG synchrony during depression is reproduced in general terms in all frequency domains. This
241 indicates a deep deprivation in depressions of frontal-occipital, frontal-temporal and interhemispheric interactions
242 throughout in sagittal direction.

243 There is a general decrease in sagittal directions with signs of left-sided asymmetry. This indicates that
244 greater activation of right hemisphere, which causes the predominance of negative emotions in depression, maybe
245 enhanced with a greater discoordination of processes in the right hemisphere.

246 In addition, an increase in synchrony was revealed in several of axially directed intrahemispheric pairs
247 of derivations primarily in temporo-central and temporo-parietal ones. This may indicate an increase in
248 systemic coordination between auditory and somatosensory sensitivity in the primary projection areas and in the
249 associative posterior temporal and parietal zones. On the other hand, a decrease in synchrony in sagittal anterior-
250 posterior-temporal and central-parietal pairs of derivations may indicate a deprivation of systemic coordination
251 between the processes in the areas of primary projection of the auditory and tactile analyzers and the associative
252 processes of integrated perception of corresponding sensations. About the primary and associative visual areas,
253 such synchronization-desynchronization phenomena are not observed.

254 It should be particularly noted that a similar picture of differences in norm and pathology was also revealed
255 in the study of schizophrenia, where there was also an extended interhemispheric and premedialsagittal zone
256 of decreased synchrony from the forehead to the back of the head with a compensatory increase in correlation
257 synchrony in axially conjugated pairs of derivations. This indicates the similarity of changes in synchrony of
258 neurophysiological activation processes in these two types of mental disorders.

259 This similarity of changes looks even more convincing considering that the topography of correlation synchrony
260 distribution in the group of healthy adolescents had significant differences from the group of healthy older adults.
261 This suggests that MEC detects similar changes in different forms of pathology and in different age groups. This
262 stability compares favorably with the heterogeneity of the results obtained when using coherence function in
263 studies of depression and schizophrenia.

264 In discriminant classification, the use of δ , θ , α 2 frequency domains allows to accurately separate the records
265 of two studied groups without any errors. Recall that δ , θ domains were also the best ones for classification of
266 schizophrenia, which once again confirms the stability of MEC results The only alternative classification of norm
267 and depression using estimates of spectral power and coherence [18] was accompanied by 8.7% of errors.

268 The material included many hours of sleep recordings for 15 right-handed men aged 18-34. Seventy-five 20-
269 second fragments were visually selected for each of 5 sleep stages W, 1, 2, 3/4, REM according to Rechtschaffen-
270 Kale criteria. The five PS matrices calculated from these fragments were the source material for subsequent
271 cross-analysis.

272 In addition to numerous particular regularities, the following significant results were obtained: 1) lefthemis-
273 sphere dominance in all stages of sleep, which is natural for right-handed subjects and indicates the effectiveness
274 of MEC; 2) the dominance of the frontal regions over the occipital ones; 3) differences in the synchrony ratios for
275 sleep stages in different frequency domains; 4) differences in the patterns of synchrony changes in interhemispheric
276 connections from the forehead to the occipital ones; 5) topographic features of localization of highly synchronous
277 connections by sleep stages and frequency domains; 6) significant topographic difference of W stage from other
278 stages; 7) close topography is observed: in δ domain for all stages; as well as in stages 2 and 3/4 for all
279 frequency domains. c) Depression [10] sophisticated methods -see in Section VIIa. It should d) Sleep stages [11]
280 Medical Research Volume XXI Issue III Version I Discriminant classification with expanded data matrices, when
281 amplitude were added to PS matrices, revealed an average of 11% errors, and classification errors of individual
282 stages were in the range of 3-20%. This is significantly better than the results of four similar publications using
283 other methods, where the classification errors of various stages were 5-42% [19][20][21][22].

284 Additionally, a control check was performed when the records of each sleep stage were divided into two groups
285 in the ratio of 80 to 20% -a learning and a classified sample. The number of classification errors of the learning

11 CONCLUSION

286 sample was 7%, and the attribution errors of the classified sample were 18.3%. This seems to be a completely
287 acceptable result, which is absent in other publications.

288 **10 VIII.**

289 **11 Conclusion**



13

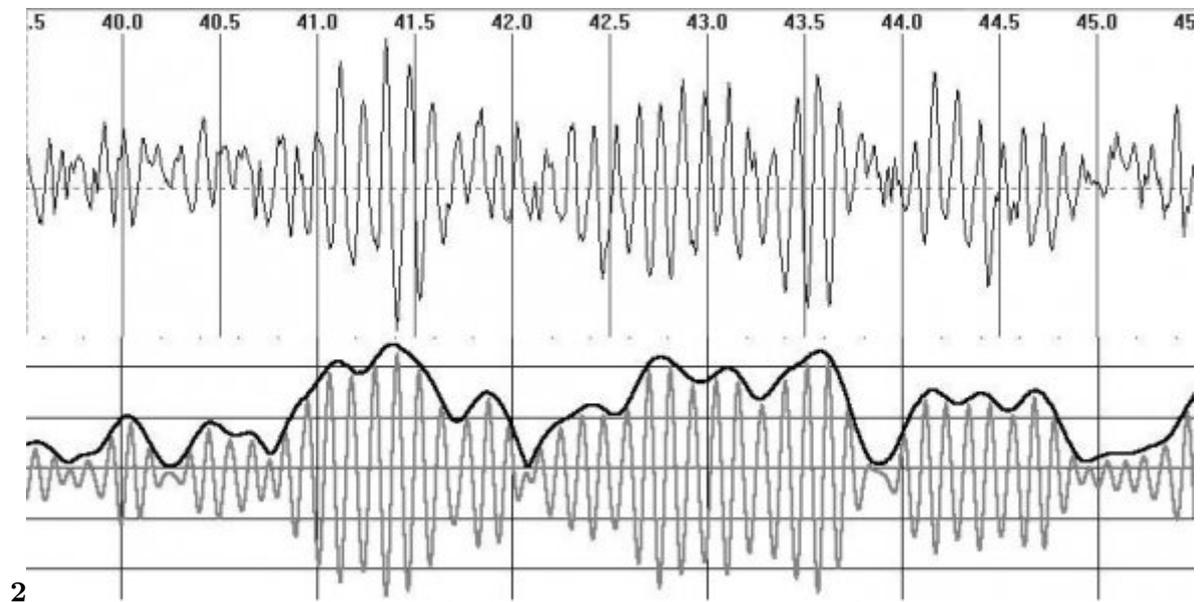
Figure 1: Fig. 1 : 3 3

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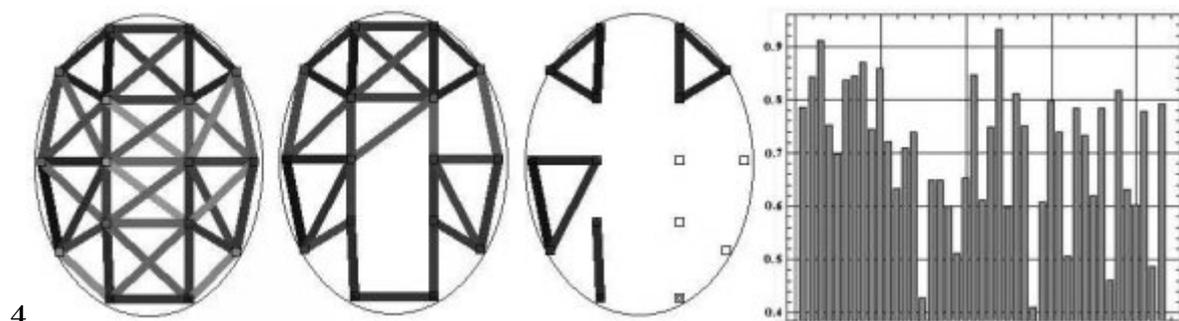
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²e.g., F L region comprising the synchrony values between F7, F3, T3, C3 derivations; C L , region including synchrony between T3, C3, T5, P3; O L region including synchrony between T5, P3, O1, etc.



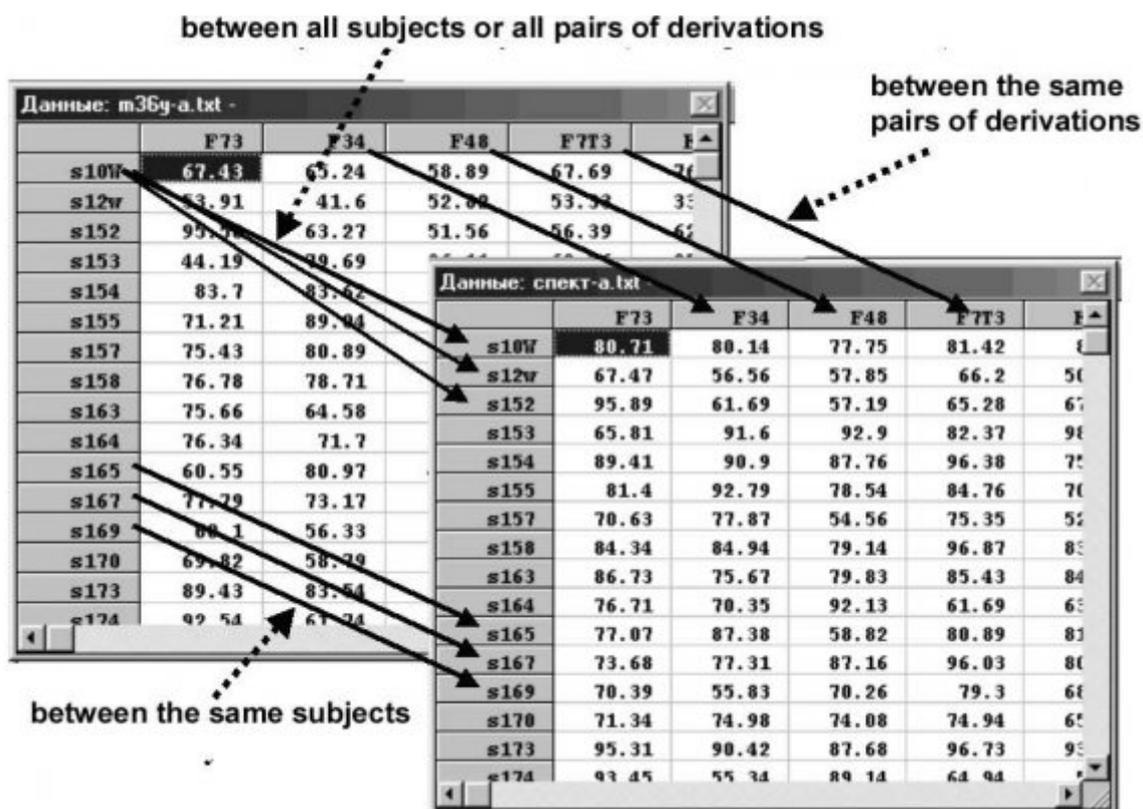
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Figure 2: Fig. 2 :



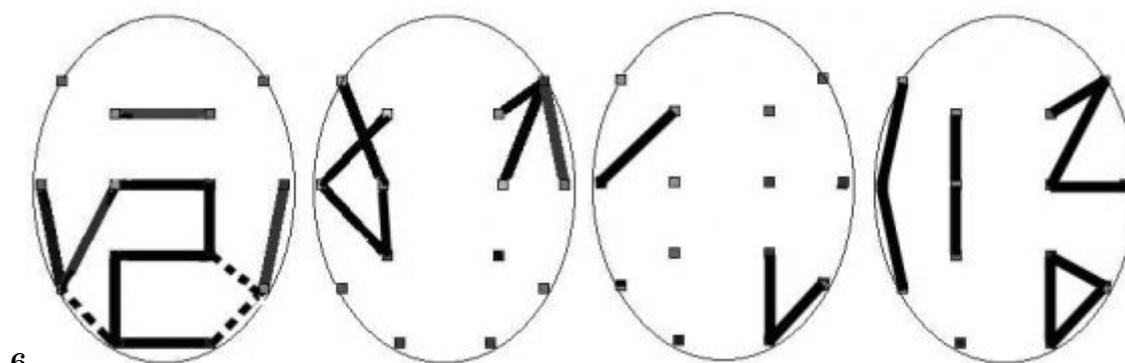
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Figure 3: Fig. 4 :



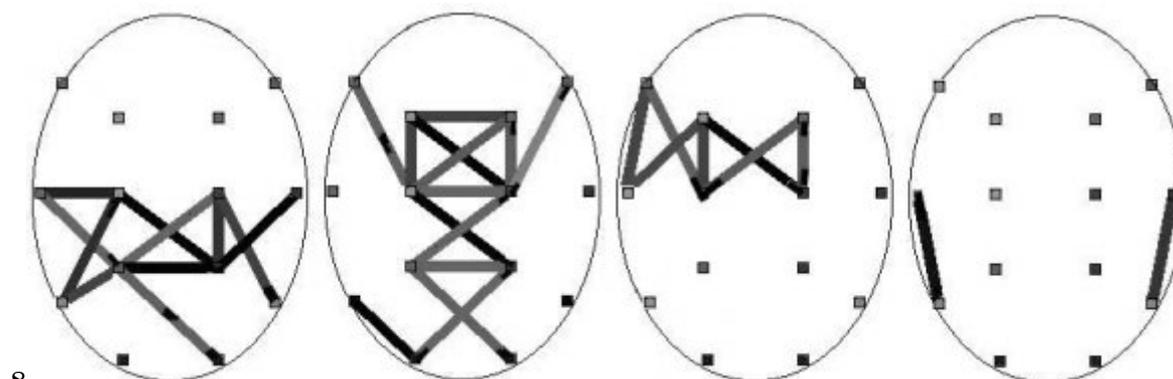
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Figure 4: Fig. 5 :



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Figure 5: Fig. 6 :



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Figure 6: Fig. 8 :

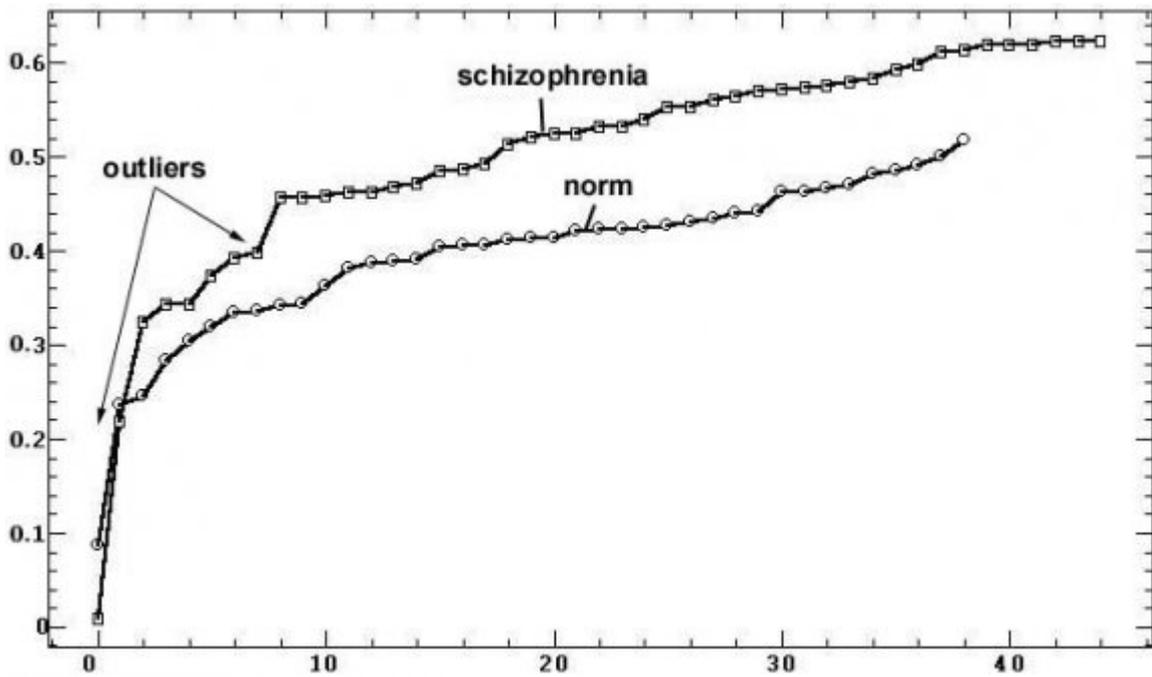


Figure 7: 58

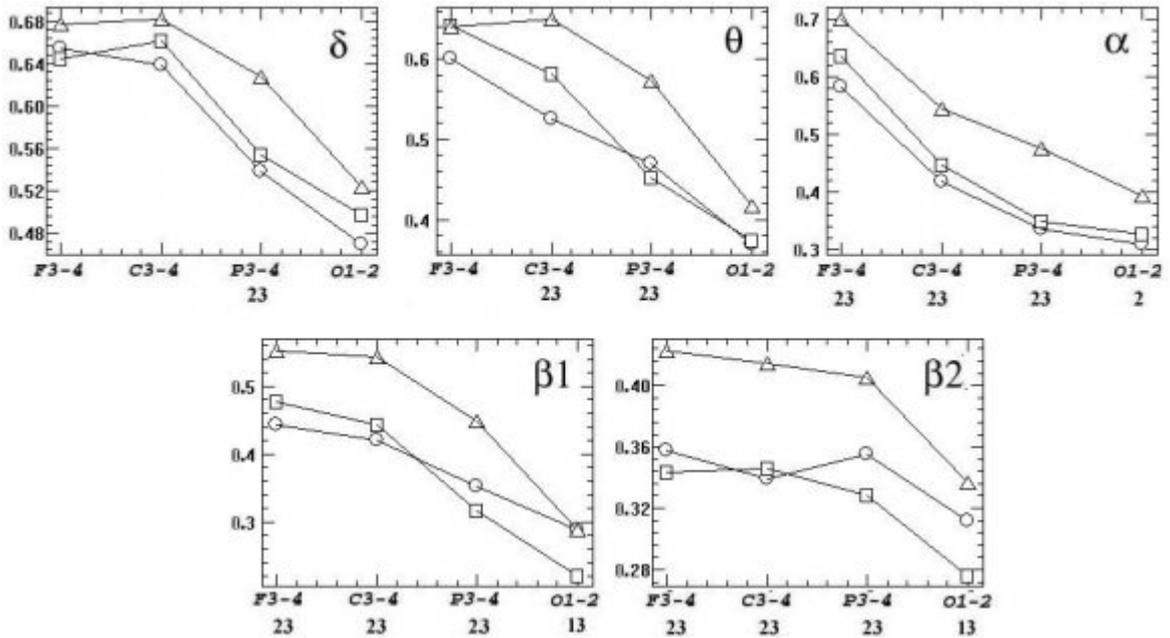


Figure 8:

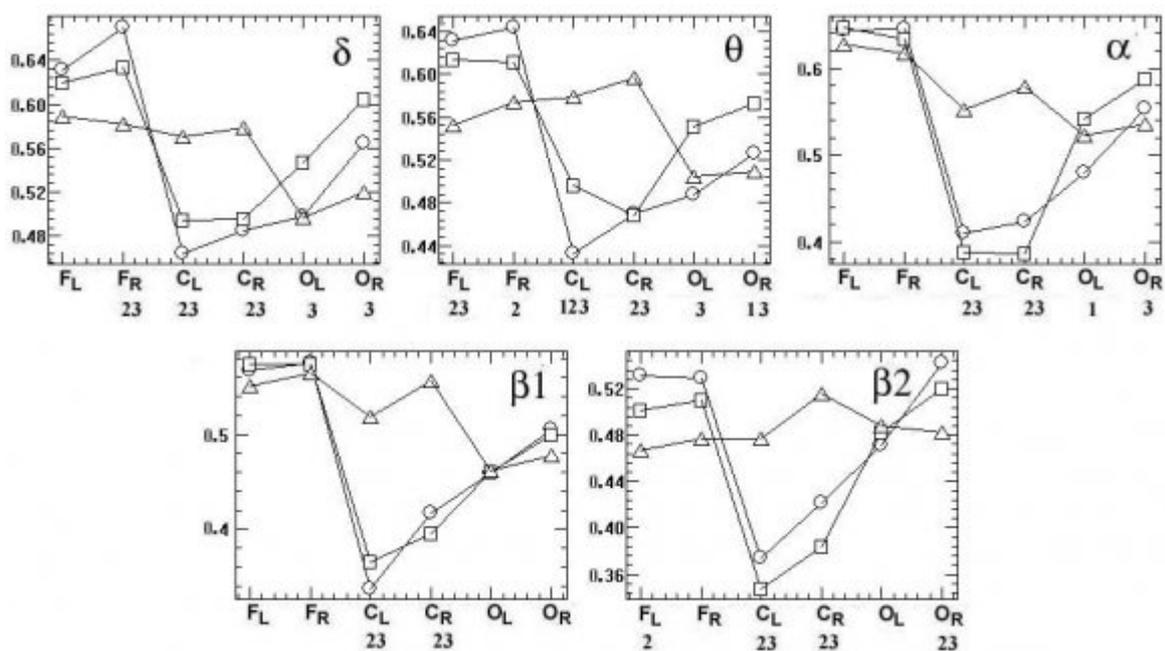


Figure 9:

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