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EEG reactivity and EEG activity in never-treated acute schizophrenics, measured with spectral parameters and dimensional complexity

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Summary. Our approaches to the use of EEG studies for the understanding of the pathogenesis of schizophrenic symptoms are presented. The basic assumptions of a heuristic and multifactorial model of the psychobiological brain mechainsms underlying the organization of normal behavior is described and used in order to formulate and test hypotheses about the pathogenesis of schizophrenic behavior using EEG measures. Results from our studies on EEG activity and EEG reactivity (= EEG components of a memory-driven, adaptive, non-unitary orienting response) as analyzed with spectral parameters and "chaotic" dimensionality (correlation dimension) are summarized. Both analysis procedures showed a deviant brain functional organization in never-treated first-episode schizophrenia which, within the framework of the model, suggests as common denominator for the pathogenesis of the symptoms a deviation of working memory, the nature of which is functional and not structural.

Keywords: Schizophrenia, EEG-reactivity, dimensional complexity, orienting reaction.

Introduction

Numerous studies reported differences in various characteristics of brain electric activity between schizophrenics and normal controls using spectral analysis (e.g., Galderisi et al., 1992; Günther et al., 1988; Itil, 1977; John et al., 1988; Karlson et al., 1987; Koukkou, 1980, 1982; Koukkou and Manske, 1986; Michel et al., 1993; Miyauchi et al., 1990; Morstyn et al., 1983). There is, however, no general agreement about the specificity of these findings for schizophrenia, and there is no agreement on the functional significance of such findings for research and practice concerning pathogenesis, diagnosis, prognosis and treatment of schizophrenia (Shagass, 1987).

In studies of non-linear systems dynamics, measurements of signal properties have become available that can assess other than spectral values of the EEG signal. One of these approaches, the correlation dimension ("D2") or dimensional complexity measures the complexity of a wave form. In recent years, the correlation dimension of the EEG has been studied in various spontaneous and induced, normal and pathological brain states (Babloyantz et al., 1985; Dvorak et al., 1986; Mayer-Kress and Layne, 1987; Rapp et al., 1989; Röschke and Basar, 1989).

When applying EEG measures in the study of the relationships between brain function and/or dysfunction and normal and/or abnormal mental states, there is a need for clarification of the basic assumptions of the general theory and the specific hypothesis to be tested with the brain's electrical activity. The experimental design and data interpretation in our EEG studies of brain functioning in schizophrenia are based on a system's theory-based psychobiological model of brain functioning (Koukkou and Lehmann, 1983, 1987a, b, 1993; Lehmann and Koukkou, 1990). The model originated from an integration of data from different disciplines concerned mainly with the brain's information processing operations that underlie the allocation of attention. Data from brain electrophysiology, cognitive phychology and psychopharmacology were specifically considered as well as data from work concerning the orienting response in humans. The model focuses on memory-driven and state-dependent brain functional mechanisms for the organization of behavior in normal and psychopathological states; it is centered around the concept of multifactorially determined brain functional states that are manifested in the scalp EEG. The specific proposals of the model are:

(1) The functional state of the brain as reflected in its electric field defines the momentarily accessible memory stores and thus, the mnemonic contents (contents of the working memory) that are accessible to the memory-driven information processing operations for the organization of behavior (state-dependent information processing).

(2) A brain state implies a certain level of organization and a dynamic balance of neural activity. This organization is multifactorially determined and is continuously and dynamically readjusted (functional adaptation) via the memory-driven pre-attentive information processing operations which underlie the initiation of a non-unitary adaptive orienting response and its "habituation" (allocation of attention). This readjustment corresponds to the updating of the working memory's contents in response to the received and initially analyzed information. The readjustment is manifest in the EEG reactivity, i.e., the EEG components of the adaptive orienting response. The dynamics of this readjustment reflect the interaction between the momentary level of coordination of the general determinants of the brain's functional state (age, vigilance, hormonal/metabolic/transmitter balance), and the kind of internally and externally originating information.

(3) A given degree of coherent coordination among the determinants of the brain's functional state corresponds to the EEG states during adequately orga-

nized behavior. This implies accessibility of age- and state-adequate memory stores and is the prerequisite for a state-adequate updating of the working memory's contents which enables a reality-oriented interaction of the individual with his environment.

Based on the proposals of this model we tested in several studies the hypothesis that acute first-episode, never-treated schizophrenics show deviations of EEG activity and EEG reactivity that suggest access to situation-inadequate memory stores (working memory contents) for the organization of behavior. The present paper summarizes results of two studies on EEG activity and EEG reactivity in never-treated first-episode schizophrenics as analyzed with two EEG analysis procedures: (1) Fourier transformation-based spectral analysis, and (2) analysis of the dimensional complexity (the correlation dimension).

Methods and subjects

Experimental design

The data were collected in the two studies with the following design: The subjects were comfortably seated in a Faraday chamber with a window for visual contact. The EEG was continuously recorded. The recording protocol included EEG epochs during resting and after presentation of auditory information to provide constraints on brain state and to make it possible to assess the EEG reactivity. The subject was instructed about the procedure and told that in general, the eyes should be kept closed and that after an initial resting period (condition I) there would be a request to open and to close the eyes again (condition II) as well as that meaningless short sentences (condition III) would be heard on a loudspeaker, and that after the recording, the subject would be asked about possible recall of the sentences. The meaningless German sentences consisted of regular words (two nouns and two verbs, of the type: "horses are counting, the lamp is breeding"). The time interval between stimuli was 2–3 min. The studies met the requirements of the Ethics Committee of the hospitals.

EEG spectral parameters, study 1

New admissions to the University Hospital of Psychiatry Zurich, presenting with a first episode of productive schizophrenic symptoms were examined before any treatment. All patients were hospitalized because of the general severity of their positive schizophrenic symptoms. The final diagnosis at discharge was schizophrenic disorder of the disorganized type (DSM-III, 295.1) or undifferentiated type (DSM-III, 295.9). As control groups we used normals, neurotics and individuals in a complete clinical and social remission after a first schizophrenic episode (= remitted schizophrenics). The neurotics were recruited via the records of the Department of Psychosocial Medicine of the University Hospital, Zürich. All subjects were drug-free, i.e., the acute schizophrenics were never treated, or, in the case of remitted schizophrenics and neurotics, they were recorded two months after termination of medication; all were self reported right-handers.
Data from 85 subjects were available for this study: 22 never-treated acute schizophrenics (8 females, 14 males, age 25.8 ± 5.7 years), 22 remitted schizophrenics (8 females, 14 males, age 26.3 ± 4.2 years), 21 neurotics (8 females, 13 males, age 29.7 ± 4.7 years), and 20 normal controls (6 females, 14 males, age 26.7 ± 3.8 years).

The EEG was recorded (bandpass 0.5–70 Hz) on FM tape from the temporal-parietal and parietal-occipital region of the left hemisphere (derivations T3-P3 and P3-01 of the 10/20 system). The data thus are the time-varying local gradients of the brain's electric field in these two regions. All data were visually edited for artifacts, and A/D converted at 256 s/sec/channel. The EEG data were Fourier-transformed using a hanning window, and power spectra were computed for analysis epochs of 4 sec.

For each subject, the power spectra were computed for 6 analysis periods: (0) for 80 sec of resting EEG (condition I, (1) for 20 sec after eye closure (condition II) and (2) (3) (4) (5) for the first and second 20 sec after the sentences # 1 and # 2 of condition III. Mean power values and centroid frequency values were computed for the delta/theta band (2–7.75 Hz), alpha band (8–12.75 Hz) and beta band (13–26 Hz).

The five differences of the values between period (0) and periods (1), (2), (3), (4) and (5) were computed as EEG reactivity, now called reactivity (1), (2), (3), (4) and (5), and used for further analysis. For other details see Koukkou and Manske (1986) , and Koukkou-Lehmann (1987).

EEC spectral parameters, study 2

The acute schizophrenics were recruited from the new admissions at the Psychiatric University Hospital of Bern in a screening procedure for admissions who presented with a first episode of productive symptoms before any treatment, and who were classified retrospectively after DSM-III 295.1 and 295.9. 26 subjects participated in this study: Eight acute schizophrenics (3 females, 5 males, age 24.6 ± 6.3 years) and 18 healthy controls (8 females, 10 males, age 29 ± 4.8 years). The EEG was recorded from electrodes attached at 19 locations of the 10/20 system. Linked earlobes (each via a 10 kOhm resistor) were used as recording reference. The data were digitized using the BioLogic Brain Atlas (sampling rate 128 Hz, analog bandpass 1–30 Hz, notch filter at 50 Hz). Artifact-free 2 sec epochs were visually identified, recomputed against the average reference and then transformed into the frequency domain by fast Fourier transformation (resolution 0.5 Hz, 0.5–31.5 Hz). For the present review, we consider only the resting periods (period 0) and the periods immediately after the four stimulus sentences of condition III. Mean EEG power spectra were computed from as many artifact-free two second-epochs as possible from the first 40 sec of the resting EEG period, and from the 25 sec after the presentation of the four stimulus sentences. Mean spectra were computed for each period, and the mean values for the delta/theta band (2–7.75 Hz) and alpha band (8–12.75 Hz) are reviewed here; for simplicity, the bands will be labelled as 2–8, 8–13, 13–26 Hz. The differences between the values of the resting period and the 25 sec after each of the four sentence presentations were computed as EEG reactivity for each subject, and used for further analysis.

EEG dimensional complexity

Data from 61 of the 85 subjects of study 1 were available for this analysis; their utilized EEG recordings were identical. The reduced number of subjects is due to the requirement for uninterrupted artifact-free data epochs of 20 sec for the estimation of the dimensional complexity (correlation dimension). The subjects were 15 never medicated, first episode acute schizophrenics (7 females, 8 males, age 27.6 ± 5.3 years), 12 remitted schizophrenics (8 females, 4 males, age 27.3 ± 4.6 years), 17 neurotics (7 females, 10 males, age 29.1 ± 3.8 years), and 17 controls (4 females, 13 males, age 27.5 ± 4.6 years). For final analysis, the following six epochs of 20 sec from the conditions I, II, and III were used in each subject: (1) during condition I (initial resting, during 40 sec after start of the recording), (2) during condition II (during 30 sec after the "eyes closed" command), and (3) (4) (5) (6) during condition III (during 30 sec each before and after the presentation of sentences # 1 and # 2). The correlation dimension of each data epoch was computed following Grassberger and Procaccia's (1983) algorithm (see Dvorak et al., 1986). For each subject and each channel, the median value of the correlation dimension across all six analysis epochs was computed and used for statistical analysis (for more details see Koukkou et al., 1993).

Table 1. ANOVA results of study 1: Eta squared-values and p-values of the ANOVA's for global differences between reactivities of the four subject groups: acute schizophrenics, remitted schizophremics, neurotics and controls, for the two EEG parameters of power and centroid frequency, the two channels and the three frequency bands. Only p values equal or smaller than 0.20 are entered. The tested data are illustrated in Fig. 1

	Power										Centroid Frequency									
	Temp.-Par.					Par.-Occip.					Temp.-Par.					Par.-Occip.				
period #	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
	2–8 Hz Band																			
eta^2	–	–	–	–	–	8	–	5	–	–	–	–	–	–	9	10	–	7	13	13
p	–	–	–	–	–	0.07	–	0.20	–	–	–	–	–	–	0.05	0.03	–	0.10	0.01	0.01
	8–13 Hz Band																			
eta^2	15	–	–	–	–	18	13	7	12	13	18	6	7	12	6	18	7	10	9	10
p	0.00	–	–	–	–	0.00	0.01	0.09	0.01	0.01	0.00	0.17	0.15	0.01	0.17	0.00	0.13	0.03	0.05	0.03
	13–26 Hz Band																			
eta^2	9	–	–	–	–	12	–	–	–	–	–	7	14	–	–	–	–	5	8	6
p	0.05	–	–	–	–	0.01	–	–	–	–	–	0.16	0.00	–	–	–	–	0.20	0.06	0.12

Results

EEG spectral parameters

For the four subject groups of study 1, Fig. 1 shows the mean values of the 5 EEG reactivity measures for power and for centroid frequency in the three EEG frequency bands (see also Koukkou-Lehmann, 1987 for further details of this study). An analysis of variance (4 groups) was done for each spectral reactivity measure, frequency band, and channel, yielding the eta square-values and p-values shown in Table 1; all p-values are double-ended. About one third of these 60 global ANOVAs showed significant differences between the four groups, but the different frequency bands and the two spectral variables (power and centroid frequency) of each band were not equally involved in these differences, suggesting different functional significances of the complex signal of the brain's electrical activity in normal and abnormal behavior. We note that the ANOVA p-values (Table 1) indicated far fewer global differences between the groups in the delta/theta and beta bands than in the alpha band.

Pairwise comparisons within and between groups further differentiated these results:

– Within groups: about 50% of all 240 tests of the EEG reactivities (Fig. 1) showed $p < 0.05$ (Table 2). Almost all reactivities of the controls and most reactivities of the neurotics were significant in the delta/theta and alpha band, for power and centroid values. Contrariwise, measured with power, only 3 of the 10 reactivities of the acute schizophrenics and 2/10 of the remitted schizophrenics were significant in the delta/theta band, and likewise only 3/10 (2/10) in the alpha band; the acute patients even showed a tendency to power reactivity in the reverse direction. Measured with centroids, the acute schizophrenics showed an ectropic, dissociated character of their EEG reactivity: 7 of the 10 reactivities were significant in the delta/theta band, comparable to the other three groups; but in the alpha band, the acute schizophrenics showed only one significant reactivity, in contrast to the clear reactivities (up to 9/10) of the other three groups (including remitted schizophrenics). – Significant reactivities in the beta band were few in all groups, with the exception of the temporal-parietal centroids where 3/5 were significant for both the neurotics and the controls, and only one for the acute patients.

– Between groups: the most frequent and striking significances were found in the alpha band (Fig. 1 and Table 3). Concerning alpha power reactivity, the acute schizophrenics and the remitted schizophrenics both differed significant-

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Fig. 1. Magnitude and direction of the EEG reactivities (differences between resting and the five post-stimulus data periods) in study 1 (Koukkou and Lehmann, 1987), for the two EEG parameters: power and centroid frequency, the two channels, the five reactivity periods (horizontal) and the four subject groups [*S* acute schizophrenics (open squares), *R* remitted schizophrenics (open circles), *N* neurotics (dots), *C* controls (crosses)]. See Table 1 for significance values

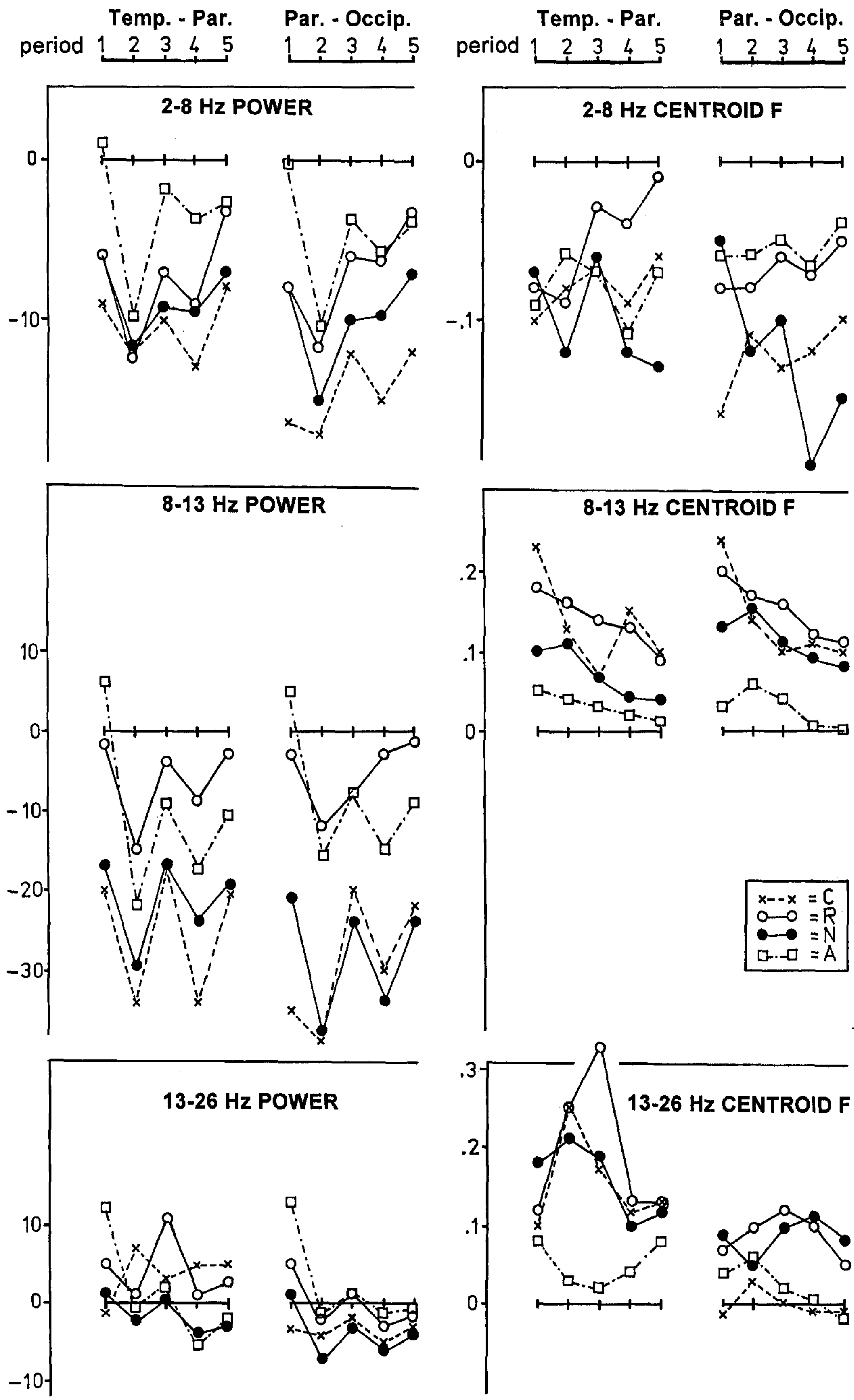
Temp. - Par.
Par. - Occip.
period 1 2 3 4 5
2-8 Hz POWER
2-8 Hz CENTROID F
8-13 Hz POWER
8-13 Hz CENTROID F
13-26 Hz POWER
13-26 Hz CENTROID F
x--x = C
o—o = R
●—● = N
□--□ = A

Table 2. Within-groups significances (double-ended p-values) of the EEG reactivities (differences between resting and the five post-stimulus data periods) in study 1, for the two parameters (power and centroid frequency), the two channels, the five reactivity periods and the four subject groups (S = acute schizophrenics, R = remitted schizophrenics, N = neurotics, C = controls). Only p values better than 0.06 are listed. See Fig. 1 for magnitudes and directions

	Power										Centroid Frequency									
	Temp.-Par.					Par.-Occip.					Temp.-Par.					Par.-Occip.				
period #	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
	2–8 Hz Band																			
S p	–	0.00	0.05	–	–	–	0.04	–	–	–	0.00	0.01	0.02	–	–	0.01	0.01	0.01	–	0.02
R p	–	–	–	–	–	0.02	0.04	–	–	–	0.00	0.00	0.05	–	–	0.00	0.02	0.04	0.02	–
N p	–	0.00	0.00	0.02	0.02	0.00	0.00	–	–	–	–	0.02	–	–	–	–	0.04	0.04	0.00	0.02
C p	0.02	0.00	0.01	0.00	0.00	0.00	0.00	–	0.01	0.05	0.00	0.04	0.02	0.00	0.00	0.00	0.06	0.02	0.01	0.04
	8–13 Hz Band																			
S p	–	0.00	0.04	–	–	–	0.01	–	–	–	–	–	–	–	–	–	0.04	–	–	–
R p	–	0.02	–	–	–	–	0.04	–	–	–	0.00	0.00	0.00	0.02	–	0.00	0.01	0.01	–	–
N p	0.00	0.00	0.00	0.02	–	0.00	0.00	0.01	0.00	–	0.00	–	0.00	–	–	0.00	0.00	0.00	–	–
C p	0.04	0.00	0.00	0.00	0.00	0.06	0.00	–	0.01	–	0.00	0.01	0.02	0.00	0.00	0.00	0.00	0.02	–	0.00
	13–26 Hz Band																			
S p	0.04	0.02	–	–	–	0.00	–	–	–	–	0.05	–	–	–	–	–	–	–	–	–
R p	–	–	0.02	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
N p	–	–	–	–	–	–	0.05	–	–	–	0.04	0.01	0.05	–	–	0.02	–	0.02	–	–
C p	–	–	–	–	–	–	–	–	–	0.05	0.00	0.02	0.05	–	–	–	–	–	–	–

Table 3. Significances of contrasts (double-ended p-values) between groups (S = acute schizophrenics, R = remitted schizophrenics, N = neurotics, C = controls) of the EEG reactivities (differences between resting and the five post-stimulus data periods) in study 1, for the two parameters (power and centroid frequency), the two channels, the five reactivity periods. Only p values better than 0.10 are listed. See Fig. 1 for magnitudes and directions

	Power										Centroid Frequency									
	Temp.-Par.					Par.-Occip.										Temp.-Par.			Par.-Occip.	
period #	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
	2–8 Hz Band																			
S vs R	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
S vs C	–	–	–	–	–	0.03	–	0.09	–	–	–	–	–	–	–	0.00	–	0.02	–	0.08
S vs N	–	–	–	–	–	0.05	0.07	–	–	0.04	–	–	–	–	–	–	–	0.00	0.00	0.06
R vs C	–	–	–	–	–	–	–	–	–	0.10	–	–	–	–	–	0.01	–	0.08	–	–
R vs N	–	–	–	–	–	–	–	–	–	0.10	–	–	–	–	0.04	–	–	0.01	0.01	0.01
N vs C	–	–	–	–	–	–	–	–	–	–	–	–	–	–	0.05	0.01	–	–	0.10.	0.08
	8–13 Hz Band																			
S vs R	–	–	–	–	–	–	–	–	–	–	0.00	0.00	0.00	0.02	0.08	0.00	0.00	0.00	0.00	0.00
S vs C	0.00	–	–	–	–	0.00	0.05	0.10	–	–	0.00	–	–	0.00	0.03	0.00	–	–	0.02	0.01
S vs N	0.00	0.05	0.02	0.05	0.02	0.00	0.00	0.00	0.00	0.00	–	–	–	–	–	0.01	0.01	0.00	0.05	0.01
R vs C	0.05	–	–	0.01	0.04	0.01	0.01	–	0.01	0.00	–	–	–	–	–	–	–	–	–	–
R vs N	0.08	0.05	0.02	0.05	0.00	0.02	0.00	–	0.00	0.00	0.06	–	0.04	–	–	–	–	0.00	–	–
N vs C	–	–	–	0.04	–	–	–	–	–	–	0.01	–	–	–	–	0.01	–	–	–	–
	13–26 Hz Band																			
S vs R	–	–	–	–	–	–	–	–	–	–	–	0.02	0.00	–	–	–	–	–	–	–
S vs C	0.03	–	–	–	–	0.01	–	–	–	–	–	0.10	0.08	–	–	–	–	–	–	–
S vs N	–	–	–	–	–	0.01	0.04	0.09	0.01	0.02	0.05	0.01	0.00	–	–	–	–	0.02	0.04	0.08
R vs C	–	–	–	–	–	0.09	–	–	–	–	–	–	–	–	–	0.04	–	–	–	–
R vs N	–	–	0.04	–	0.01	0.07	0.07	–	–	–	–	–	–	–	–	–	–	–	–	–
N vs C	–	–	–	–	0.05	–	–	–	–	–	–	0.05	–	–	–	0.04	–	0.10	0.01.	0.01

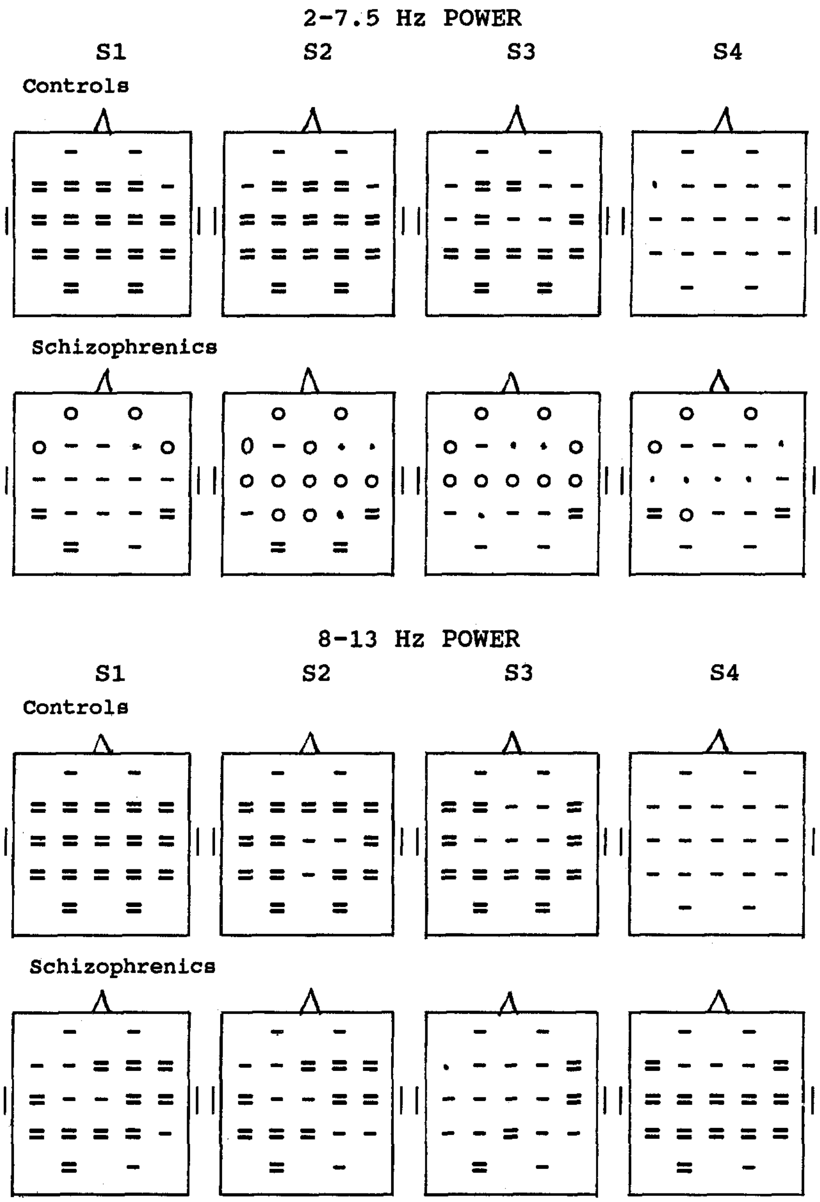

Fig. 2. Directions and significances of the mean EEG reactivities to the four sentence presentations (S1, S2, S3, S4) of schizophrenics (N = 8) and controls (N = 18) in study 2. 19-channel recordings. Schematic display, head seen from above, nose up, left ear left. Mean reactivities consisting of decreased values after the stimulus are indicated by (–) and (=) signs, increased values by (o) and (O) signs. (=) and (s) indicate significances better than p = 0.05. Mean differences below cut-off indicated by (·)

ly from the neurotics and the controls in the temporo-parietal as well as in the parieto-occipital channel; the controls and neurotics had stronger reactivities. The centroid reactivitiy in the alpha band, however, separated the acute schizophrenics from the other three groups (remitted schizophrenics, neurotics and controls) who had stronger centroid reactivities. Fewer differences of reactivity were significant in the delta/theta and in the beta band for power and centroids.

An overview of some results of study 2 is shown in Fig. 2. The figure illustrates the spatial distribution, the direction and the significances of the sentence-induced reactivity of power values in the delta/theta and alpha band in the acute schizophrenics and the controls. Similar to the results of study 1, there were distinct differences of reactivity between the groups. Generally, the data suggest that schizophrenics EEG reactivity in comparison with normal reactivity is not only characterized by fewer power value reductions (far fewer than in normals were significant), but by a partially reverse direction and by different spatial distributions of reactivity, as well as by a differential participation of the two frequency bands.

EEG dimensional complexity

There were clear differences of the correlation dimension between groups in the temporal-parietal EEG recordings (Koukkou et al., 1992, 1993). The first episode, never-treated schizophrenics showing highest values (median = 4.44), the remitted cases and the neurotics showing intermediate values (medians = 4.18, 4.11, respectively) and the normal controls showing lowest values (median = 3.96): The Kruskal-Wallis ANOVA showed that the differences between groups were significant (N = 61, chi square = 17.0, df = 3, $p < 001$). Post-hoc tests yielded significant differences between first episode acute schizophrenics vs neurotics ($2\,p < 0.002$) and controls ($2\,p < 0.004$) The remitted schizophrenics differed at $2\,p < 0.16$ from the first episode schizophrenics and at $2\,p < 0.20$ from controls; the neurotics did not differ significantly from remitted cases and controls. On the other hand, there was no overall significant difference between the subject groups in the parietal-occipital EEG recordings.

Discussion

As mentioned in Introduction, the specific hypothesis tested with our EEG studies is that humans who are in a first episode of schizophrenic symptoms display a deviant (ectropic) functional organization of the neural activity as manifested in the scalp EEG activity and particularly, in their EEG reactivity, i.e., in the EEG components of the orienting response. The results of the two independent populations and the two analysis procedures support this hypothesis.

The power spectral analysis showed that the brain's functional organization as measured with the EEG reactivity is deviant (ectropic) in acute schizophrenics as compared with remitted schizophrenics, neurotics and normals. This deviation consisted of a two-faced orientation – a dissociation – of the EEG components of an adaptive orienting response in which different EEG frequency bands and different spectral EEG parameters of each frequency band (mean power and centroid frequency) were differently involved in the acute patients; remitted schizophrenics showed a partially normalized EEG reactivity (Koukkou et al., 1982; Koukkou-Lehmann, 1987). Within the framework of our model, the EEG spectral signs of schizophrenics suggest deviations of the updating of the working memory's contents. This deviant updating indicates a simultaneous access (1) to developmentally earlier memory stores (as indicated by the reactivity of EEG slow waves) and thus, access to contents and strategies of thinking conceivably related to those seen during hypnagogic hallucinations, and (2) to age- and state-corresponding memory stores (indicated by "no reaction" or by differently distributed reactions within the alpha band) and thus, access to adult, wakekful strategies of thinking. This dissociated brain functional state in schizophrenia accounts with its dual aspect for the co-existence of the characteristics of reality-remote, only loosely controlled percepts and thought concatenations and the simultaneous possibility of reality-oriented mentation and behavior as it is observable in the patient's daily activities.

The computation of the dimensional complexity of the EEG brain mechanisms, i.e., the use of a method that measures properties of the EEG that are not directly related to the results of spectral analysis (and that we used in a comparative way) gave a novel perspective to EEG data in schizophrenia, and brought further support of a different brain functional organization in schizophrenia. We found a higher dimensional complexity of functional brain mechanisms in schizophrenics versus normals in the left temporal-parietal brain region and no overall significant differences between the groups in the left parietal-occipital EEG (Koukkou et al., 1992, 1993) Thus, an increased dimensional complexity was found in the EEG in one of the two examined brain regions in the acute, never treated schizophrenics. This finding can be understood as loosening of the coordination between the active brain processes in schizophrenics compared with normals. The finding of increased dimensional complexity of the EEG in one brain area of the acute schizophrenics is in line with the concept of a dissociated functional EEG state with its two-faced orientation as proposed by the analysis of the EEG's spectral parameters.

The deviations of the brain's functional organization that we found in the schizophrenics' EEG with the two analysis procedures cannot be drug effects or chronicity effects since we have analyzed the EEG of acute patients who were never treated and were in a first episode. Thus, the findings indicate that these deviations accompany or relate to the pathogenesis of the symptoms.

The wide range of deviant experiences and behavior, i.e., the symptoms that lead to the diagnosis of schizophrenia are not pathognomonic for schizophrenia since they appear also in other diseases. Thus, research on the pathogenesis of schizophrenia has to distinguish between the pathophysiological mechanisms leading to the predisposition to the symptoms and the pathophysiological mechanisms leading to the manifestation of the symptoms. The results of our studies and their interpretation within the framework of our model refer mainly to the latter, the manifestation. Thus, our model links together all the symptoms of schizophrenia and accounts for their unspecifity by proposing that they result from accessibility of inadequate memory store.

Within the discussed model of brain functional mechanisms that considers EEG state-dependency of the memory-driven brain information processing, our findings suggest the following: Given that the two EEG analysis procedures assess the level of organization of the brain's functional state, and given that the brain's functional state reflects the momentarily accessible memory stores (the contents of the working memory), the characteristics of EEG activity and EEG reactivity of normals describe the level of dynamic coordination among the general determinants of the brain's functional organization which enable the accessibility of state-adequate memory stores (working memory content) as well as the state-adequate updating of these contents. The EEG deviations in schizophrenics indicate non-coherent (state-inadequate) lovels of coordination among the determinants of the brain's functional organization. This means, within the framework of our model, that schizophrenic symptoms are accounted for by the patient's "ability" to access during wakefulness situation-inadequate memory stores due to the inadequate updating of the contents of working memory (compare Koukkou et al., 1991). Research on the pathogenesis of these deviant EEG states in schizophrenia has to consider possible deviations in determinants of the brain's functional state as well as of the brain's information processing operations which underlie their dynamic coordination. Our model suggests, however, that the common denominator of the pathogenesis of the smptoms is the accessibility of state- and/or age-inadequate memory stores. This indicates a functional and not a structural deviation of working memory.

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