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Original Articles

Hypofrontality on Topographic EEG in Schizophrenia

Correlations with Neuropsychological and Psychopathological Parameters

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Summary. Topographic EEG was performed in 17 DSM-III-R schizophrenic patients and in 15 sex- and age-matched healthy controls. Eleven patients were first-onset (neuroleptic naive) schizophrenics. EEG band power was compared with psychopathology, neuropsychology and neurological soft signs. The EEG was recorded at 14 topographic locations monopolarly and movements of the eye and of the lid were monitored by two bipolar electro-oculogram (EOG) derivations, one vertical and one horizontal. A multivariate correction of EOG artefacts was performed based on regression analysis with respect to EOG channels. Schizophrenic patients showed higher mean and median power in most bands. These differences were most marked in the delta band, in the fast alpha and beta bands, in particular at left frontal sites. Delta power at F7 was by far the best separating variable between schizophrenics and controls in a discriminant analysis. Significant positive correlations were found between the Brief Psychiatric Rating Scale scores "Anxiety-depression" and "Activation" and power in the fast bands and negative ones between "Anergia" and the beta bands. Positive significant correlations emerged between the total score in the Negative Symptoms Rating Scale and the amount of delta power, predominantly over the temporal region. Impairment in the Luria-Nebraska neuropsychological scores "Rhythm" and "Memory" correlated highly significantly with EEG band power. No correlations were found between neurological soft signs and EEG band power. Our results are in line with the hypothesis of a hypofrontality in schizophrenia. It is unlikely that these findings are an artefact of prior psychiatric treatment, as they were also observed in first-onset, neuroleptic naive schizophrenics. Moreover, our data suggest that these abnormalities are of clinical and functional relevance, as they correlated significantly with psychopathological and neuropsychological parameters.

Key words: Schizophrenia – Topographic EEG – Neuropsychology

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Introduction

A large body of experimental evidence suggests the presence of brain dysfunction in schizophrenia. Schizophrenic patients were found more frequently than healthy individuals to have neuropsychological deficits, neurological "soft" signs, structural brain abnormalities, disturbances of cerebral metabolism and EEG abnormalities. These findings are predominantly related to a subgroup of patients with "process" schizophrenia, a more deleterous form of the disease and the prominence of negative symptoms (review in Seidman 1983).

In the last half century an impressive number of studies have reported qualitative and quantitative EEG abnormalities in schizophrenia (Itil 1977). A diffuse slowing of EEG and more high frequency activity have been reported, and the differences were often more pronounced in the left hemisphere (Karson et al. 1988a). Recent investigations using power spectral analysis suggest further a slowing of brain electrical activity, especially in the frontal regions (Morihisa et al. 1983; Morstyn et al. 1983; Guenther et al. 1986; Nakagawa et al. 1991; Shagass 1991). However, caution has been recommended in the interpretation of this finding, as it could result at least in part from eye-movement artefact (Karson et al. 1987).

Taking this criticism into account the present study investigated the topographic EEG in drug-free schizophrenics (most of them drug-naive) in comparison with healthy controls and sought for relationships between EEG band power and psychopathological, neuropsychological and neurological variables.

The present study had mainly an explorative character. However, based on data from the literature (Seidman 1983) we expected differences between schizophrenics and controls, especially in the slow frequencies bands, which should also be related to the clinical manifestations of "process" schizophrenia (i.e. negative symptoms and neuropsychological deficits). Moreover, according to the basic literature (Ray and Cole 1985) fast band power could be expected to relate to psychopathological scores reflecting arousal and cognitive and emotional processes.

Subjects and Methods

Subjects. The sample comprised 17 DSM-III-R paranoid schizophrenic inpatients hospitalized in the research ward of the Central Institute of Mental Health in Mannheim (12 male, 5 female; mean age 27.7, SD 6.0 years) and 15 healthy controls (8 male, 7 female; mean age 30.5, SD 8.1 years). Eleven patients were first-onset, neuroleptic-naive schizophrenics. The remaining 6 patients were drug free for at least 1 week; they had a mean duration of illness of 3.4, SD 6.0 years and a mean of 2.7, SD 1.9 previous psychiatric hospitalizations. All subjects were right-handed.

Clinical Assessments. Patients' *psychopathological state* was assessed by means of the Brief Psychiatric Rating Scale (BPRS) and the Negative Symptom Rating Scale (NSRS, Iager et al. 1985). *Neuropsychological tests* were performed using a shortened version of the Luria-Nebraska battery comprising the subscores "Rhythm", "Receptive speech", "Memory" and "Intellectual processes". *Neurological "soft" signs* were examined according to a modified version of the instrument proposed by Quitkin et al. (1976).

EEG Recording. The EEGs were recorded at 14 topographic locations monopolarly against linked shunted earlobes as a reference (F7, F3, F4, F8, C3, Cz, C4, T3, T4, T5, T6, Pz, O1, O2). In addition, movements of the eye and of the lid were monitored by two bipolar electro-oculogram (EOG) derivations, a vertical and a horizontal one. When the subject was quiet, 120 s of EEG at rest, eyes closed, were recorded and digitized on-line (sampling frequency 200 Hz).

Statistical Processing. Out of 120 s recorded 11 overlapping epochs of 20 s were formed and the "best" epoch of 20 s was selected for quantitative analysis. Automatically, the best epoch with respect to eye artefacts was selected (minimum EOG power 1.5–7.5 Hz). This criterion, and the relatively short epoch of 20 s analysed, follow from a previous evaluation (Möcks and Gasser 1984). This selection was checked for muscle artefacts both visually and by considering power in the band (25.0–49.0 Hz) and improved when necessary.

The resulting epoch was submitted to spectrum analysis for all derivations. A multivariate correction of EOG artefacts was performed based on regression analysis with respect to EOG channels (Möcks et al. 1989). Band power was computed in the following bands: delta, 1.5–3.5 Hz; theta, 3.5–7.5 Hz; $alpha_1$, 7.5–9.5 Hz; $alpha_2$, 9.5–12.5 Hz; $beta_1$, 12.5–17.5 Hz; $beta_2$, 17.5–25.0 Hz; $beta_3$, 25.0–49.0 Hz. A log transformation was applied when appropriate (Gasser et al. 1982).

In this preliminary data analysis mainly univariate statistics were computed and group comparisons were performed by Wilcoxon tests. In order to corroborate these results a repeated measures analysis of variance was computed for each band (log power) with the between factor "group" (levels: patients, controls) and the two within factors "sagittal topography" (levels: frontal line, central line, posterior line) and "horizontal topography" (levels: outer left, inner left, inner right, outer right), yielding two crossed factors for the derivations F7, F3, F4, F8, T3, C3, C4, T4, T5, O1, O2, T6. Greenhause-Geisser correction was applied to non-conservative P values. Owing to the small sizes of the groups only weak interactions between the group factor and the topographic factors can be expected.

Spearman rank correlations were computed to assess the relations of EEG band power with BPRS scores, with negative symptoms (NSRS), with neurological soft signs and with neuropsychological deficits.

Because of the exploratory character of this study, the correlational analysis was done in a univariate way. However, it should be noted that a pattern oriented approach is followed in so far as clusters of high correlations in certain bands or in certain brain regions are interpreted in combination with the absence of stable correlations in other bands or regions. By avoiding the interpretation of single correlations, the pitfalls of a univariate analysis are largely avoided.

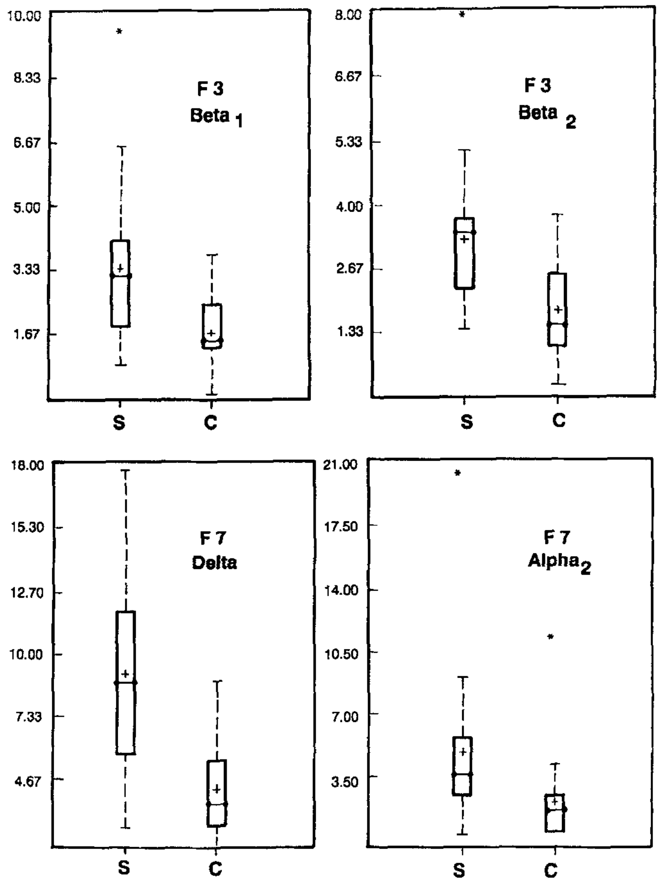

Fig. 1. Distribution of absolute band power at left frontal sites for schizophrenic patients *(S)* and healthy controls *(C)*; (•—•, median; +, mean)

Table 1. Significant differences in EEG band power between schizophrenic patients and healthy controls (*$P<0.05$; **$P<0.01$); for all differences higher band power in schizophrenics

	Delta	Theta	$Alpha_1$	$Alpha_2$	$Beta_1$	$Beta_2$	$Beta_3$
F7	**	*		**	**	**	*
F3	*			*	**	**	
F4				*			
F8							
C3						*	*
C4							*
Cz				*			*
T3	*						
T4	*						
T5				*			
T6	*						
Pz				*	*		
O1							
O2							

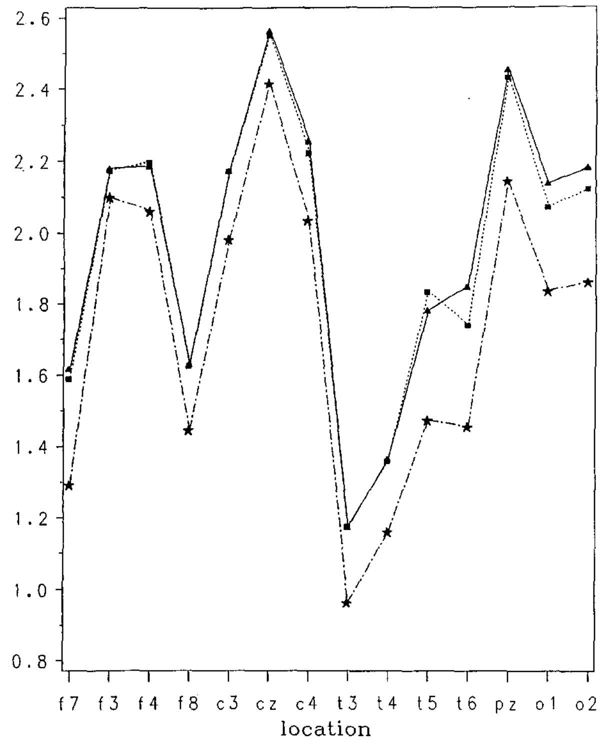

Fig. 2. Topographic profile of log-transformed delta power in the total schizophrenic group (▲), only first-onset schizoprenics (■) and healthy controls ∗

Results

Comparison of Groups

The total group of schizophrenic patients ($n = 17$) showed higher mean and median power in most bands as compared with the healthy controls. These differences were most marked in the delta band, in the fast alpha and beta bands. Variability for schizophrenic patients was also higher, pointing to a certain heterogeneity of the group in neurophysiological terms. Box plots (Fig. 1) serve to illustrate the differences in distribution between the two groups. The differences found in the univariate analysis often reached significance in statistical testing (Table 1). They were most pronounced in the left frontal area and in the temporal region for the delta band. Delta power at F7 was by far the best separating variable between schizophrenics and controls in a discriminant analysis. The fast bands showed differences mainly in the left frontal area and over the centroparietal region. The repeated measures analysis of variance showed a significant main effect ($P = 0.03$) for the delta band and statistical trends for the $alpha_2$ band ($P = 0.08$) and for the $beta_2$ band ($P = 0.08$). As expected, interactions did not reach statistical significance.

Results remained essentially the same when only the 11 first-onset, drug naive patients were compared with the controls (see Fig. 2 with a topographic profile of transformed delta power). No significant differences in band power were found between drug-naive and previously treated patients who were drug-free for at least 1 week.

Correlations

Significant positive correlations were found between the BPRS score "Anxiety-depression" and the fast band power at posterior sites. The score "Acitvation" correlated significantly with delta and beta power over the left fronto-temporal region. The score "Anergia" had significant negative correlations with fast band power in a topographically diffuse way. The scores "Thought disturbance" and "Hostile-suspiciousness" and the total BPRS score did not lead to any appreciable correlations. However, significant positive correlations emerged between the total score in the NSRS and the amount of delta power, strongest over the temporal region (Table 2).

Impairment in the neuropsychological scores "Rhythm" and "Memory" correlated highly significantly (between 0.60 and 0.70) with EEG band power, whereas correla-

Table 2. Correlations between EEG band power and psychopathological scores

	Delta	Theta	$Alpha_1$	$Alpha_2$	$Beta_1$	$Beta_2$	$Beta_3$
F7	4**		4*		4**, 5*		4**
F3	N*			1*	N*	N*, 2*	
F4	N*	N*					
F8					2*	2**	2**
C3					1*, 2**	2**	
C4	N*						
Cz	N*, 2***	2*			1*, 2*	2*	
T3	4**		4*		4**	4**	
T4			5*			1*, 2*	2*
T5	N***				1**, 2**		
T6	N**			1**, 2**	1***, 2***,3*	1*, 2***	
Pz	n*, 3*			2*	1***, 2**	2***	
O1	N**			1*	1**, 2**, 3*		N*
O2	N**			1*	1**, 2**, 3*	1*, 2**	

N, Negative Symptom Rating Scale total score; BPRS scores: 1 = Anxiety/depression; 2 = Anergia; 3 = Thought disturbance; 4 = Activation; 5 = Hostile-suspiciousness (* $r > 0.42$, $P < 0.10$; ** $r > 0.48$, $P < 0.05$; *** $r > 0.62$, $P < 0.01$).

tions were throughout negligible with the scores "Receptive speech" and "Intellectual processes". The score "Rhythm" showed this association for the theta band and the fast bands over the left frontal and the anterior temporal and occipital regions; the score "Memory", on the other hand, had even stronger relations for the same frequency bands over most of the topography.

No correlations were found between neurological soft signs and EEG band power.

Discussion

Group Differences

Schizophrenic patients in our study showed higher power in the fast bands and especially in the delta band as compared with healthy controls. These differences were not a result of previous neuroleptic treatment, as they were also observed in drug-naive schizophrenics. Moreover, the lack of differences in band power between neuroleptic naive and previously treated patients suggests that the washout period of 1 week in our sample was enough to minimize neuroleptic artefacts on EEG. This assumption however, needs, confirmation in a larger sample.

The increased band power in schizophrenics was most pronounced at the left frontal and at temporal sites. However, delta power is increased in schizophrenics in a topographically diffuse way (Fig. 2), and the clearer statistical significance at left frontal and temporal sites is not only due to large mean differences, but also to a relatively low coefficient of variation for the group of schizophrenic patients at F7, F3, T3 and T4.

When performing a quantitative analysis of the EEG at rest, spectral power is greatly increased by ocular (EOG) artefacts at the frontal derivations, in particular for the slow bands delta and theta (Gasser et al. 1986). Karson et al. (1987) stressed the importance of excluding such EOG artefacts in studies with schizophrenics, as such patients are known to exhibit more eye movements and blinking than healthy individuals (Karson 1983; Matsue et al. 1986). In our study the differences became statistically more pronounced after EOG artefacts were corrected as described in a companion paper (Gasser et al. 1992). Our finding of increased left frontal delta and theta band power in schizophrenics is in line with the findings of a hypofrontality reportd in EEG (Guich et al. 1989), cerebral blood flow (Ingvar and Franzen 1974; Paulman et al. 1990, Sagawa et al. 1990, and positron emission tomography (Buchsbaum et al. 1982) studies in schizophrenia. Our finding with respect to delta power is interpreted as a physiological dysfunction, rather than as a sign of disturbed psychological functions in terms of cognitive and emotional processing. The latter is thought to be at the root of increased fast activity, which has frequently been found in EEG studies. This interpretation is in line with neurological and psychophysiological knowledge (as to the latter compare, for example, Ray and Cole 1985, who describe specific changes in beta power both in cognitive and emotional processing). The correlations found within the group of schizophrenics with negative symptoms and with some BPRS scores as well as with neuropsychological impairment (see below) are in line with the interpretation of group differences.

Correlations Between Band Power, Psychopathology and Neuropsychology

The correlations between EEG band power and psychopathology in our patients are of interest. The two BRPS scores reflecting productive acute symptomatology (Thought disorder and Hostile-suspiciousness) do not show any sizeable correlations, and this is an interesting negative finding. The correlations between fast band power and the BPRS scores "Anxiety-depression" and "Activation" (positive correlations) as well as "Anergia" (negative correlation) are in line with the psychophysiological literature, as they are interpreted as reflecting disturbed cognitive, emotional and arousal processes. However, the topographic pattern of correlations, and in particular the concentration on the left frontotemporal region for the score "Activation", lacks a clear interpretation at present (compare also Itil et al. 1972; Morihisa et al. 1983; Karson et al. 1988b).

We found a consistent correlation between negative symptoms and delta band power (Table 2). Whereas negative symptoms are thought to be associated with a more severe form of schizophrenia, the delta band power can be considered as an indicator of pathophysiological conditions. Thus our finding is in line with the reported associations between brain dysfunction and "process" schizophrenia (Seidman 1983) and it suggests further that both negative symptoms and increased delta activity are closely related to a basic brain pathology in schizophrenia.

Neuropsychological impairment is assumed to characterize a subgroup of schizophrenic patients (Gruzelier 1991). The most frequent findings are a dysfunction of the left hemisphere and of the frontal lobe (Flor-Henry and Yeudall 1979; Taylor et al. 1979; Williamson et al. 1989), although several studies have failed to localize the abnormalities and found rather a similarity between schizophrenics and diffuse brain-damage patients with regard to neuropsychological test performance (Seidman 1983). In our sample the correlations between neuropsychological impairment and EEG power were spread across the different localizations and were related to both the slow and the fast bands. It would be too speculative to interpret such correlations in a topographic sense; the possibility that they reflect to some extent the inter-relationship between disordered brain electrical activity and neuropsychological performance should be further investigated in larger samples.

In spite of a number of studies reporting that schizophrenics have abnormal neurological signs more frequently than healthy individuals, the relationship between these findings and the disease process has not yet been established (Heinrichs and Buchanan 1988). The lack of a relationship between neurological soft signs and EEG band power in our sample is an agreement with other studies (Kennard 1960; Mosher et al. 1971; Torrey 1980) in which similar negative findings were observed.

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