Eur Arch Psychiatr Neurol Sci (1989) 239:194–209

European Archives of Psychiatry and Neurological Sciences

Psychomotor Disturbances in Psychiatric Patients as a Possible Basis for New Attempts at Differential Diagnosis and Therapy

IV. Brain Dysfunction During Motor Activation Measured by EEG Mapping*

W. Günther[1], P. Streck[1], R. Steinberg[1], R. Günther[2], L. Raith[1], and M. Backmund[1]

[1]Psychiatric University Hospital, Nussbaumstrasse 7, D-8000 Munich 2, Federal Republic of Germany
[2]Psychologisches Institut der Universität, D-7400 Tübingen, Federal Republic of Germany

Summary. In parts I–III of this series psychometric evidence was reported of a "psychotic motor syndrome" (PMS) in schizophrenic and endogenous depressed patients, which was not found in non-endogenous depressed or healthy persons. An attempt is reported to establish signs of brain dysfunction in these patient groups during motor activation, using a 16-channel EEG mapping system. "Resting" conditions after a special relaxation procedure were compared with simple and complex motor tasks (and music perception/reproduction; to be reported separately). Two measurements, at least 2 weeks apart, were obtained for each subject, in order to obtain information on the influence of drug treatment and/or psychopathological improvement on brain dysfunction. In all, 23 male and 25 female schizophrenics, 11 male and 18 female non-endogenous depressed patients (not actually medicated, i.e. drug naive or wash-out period of 1 week to 17 years), and 26 male and 37 female endogenous depressed patients (medicated with tri- or tetracyclic antidepressants and/or benzodiazepines; no lithium treatment) were compared with 22 male and 17 female control persons (i.e. total $n = 179$). Major findings were obtained in the delta and alpha frequency bands yielding signs of "diffuse hyperactivation" in schizophrenic and endogenous depressed patients as compared with the patterns found in healthy persons. However, since in the *non-endogenous* patients a (less marked) hyperactivation of various EEG parameters was also found, unspecific effects such as anxiety/arousal may have influenced the results in psychotic patients, which was to be explored further. Drug treatment tended to "normalize" the activation pattern both in schizophrenics and endogenous depressed patients. Viewing the findings on schizophrenics using neuroimaging methods [single photon emission computerized tomography-(SPECT), magnetic resonance imaging-(MRI), positron emission tomography-(PET)], these results suggest pathological brain organization connected to an impaired motor performance (evident peripherally as PMS) in schizophrenic and endogenous depressed patients. If it is possible to further "externally validate" (by SPECT/MRI/PET) EEG mapping data this method may exclusively offer the possibility of innocuous long-term follow up of brain dysfunction in psychotic patients ("brain function monitoring"). This could enable the early recognition (and early therapy) of negative symptoms. Finally, the EEG mapping findings provide further neurophysiological basis for the use of motor training programs in the additional therapy of psychiatric patients.

Key words: Motor dysfunction – Hemispheric dysfunction – Disturbed hemispheric laterality – EEG mapping in psychosis

* Supported by Deutsche Forschungsgemeinschaft (DFG Gu 207/4-1)

Offprint requests to: W. Günther

Introduction

There is increasing evidence of disturbed hemispheric functioning in endogenous psychotic patients, using psychometric (e.g. Mather and Putchat 1984), psychophysiological (e.g. Gruzelier 1985), quantitative EEG (Flor-Henry et al. 1987), "mapped" EEG (e.g. Morihisa and McAnulty 1985) and evoked potential data (e.g. Maurer and Dierks 1987), single photon (e.g. Günther et al. 1986c) or positron emission (e.g. Brodie et al. 1984) and computed tomography. Recently, there have been efforts to examine the sub-

jects not only in "resting" (eyes open/closed) conditions, but in various "activation tasks" as well (such as Wisconsin Card Sorting Test, spatial imagination, listening to music, verbal tasks).

We chose motor activation tasks for the following reasons. Motor disturbances in psychiatric patients were known long before drug therapy was introduced into psychiatric treatment, thus suggesting a disease-related syndrome (Manschreck et al. 1986; Günther et al. 1987). Our psychometric studies I–III, published in this journal previously (Günther et al. 1983, 1986a, 1988a), yielded evidence of a wide "psychotic motor syndrome" (PMS) in schizophrenic and endogenous depressed patients, consisting of disturbances of the fine and gross movements of the dominant right hand, the lip, tongue and mouth motility, and the complex coordination of the extremities.

In a series of investigations using a 16-channel EEG mapping system on *neuroleptic-treated* schizophrenics, we established signs of correlated brain dysfunction during various motor tasks with the dominant right hand. Left hemisphere hypofunction/right hemisphere overactivation was demonstrated in schizophrenic patients displaying positive symptoms. In contrast, sings of bilateral hemispheric non-reactivity were demonstrated in "negative" schizophrenic patients.

This EEG mapping evidence of brain dysfunction was further supported using single photon (Günther et al. 1986c) and positron emission (ongoing; first report by Günther et al. 1988c) computed tomography in *un*treated schizophrenic as well as drug-treated endogenous depressed patients. Similarly, in the EEG mapping study to be reported here, we studied *untreated* schizophrenic, non-endogenous depressed patients and control persons, along with *drug-treated* endogenous depressed patients using simple and complex motor activation. These were the same patient groups as in parts I–III of our series.

We attempted to establish simultaneously the quality of motor performance (using the same motor test battery as in parts I–III) and EEG mapping parameters of possible brain dysfunction. Special care was taken to measure exactly special psychopathological features of our patients, since both EEG mapping and SPECT/PET studies indicated an important influence of the "positive-negative symptom" dimension on brain dysfunction results.

Methods

Subjects

Subjects were healthy control persons (described below) and in-patients of the Psychiatric University Hospital links der Isar, Munich, selected as follows. Patients who received a preliminary clinical diagnosis of schizophrenic psychosis (ICD group 295, except 295.7), endogenous depressive psychosis, mono- or bipolar (ICD 296.1 or .3), or non-endogenous depression (ICD 300.4, depressive neurosis; 309.0/.1, short/longer-lasting depressive reaction), *and* were not actually treated with drugs for at least 1 week (exception for endogenous depressed patients: *and* were *only* treated with tri- or tetracyclic antidepressants and/or benzodiazepines) were selected for the study, when they fulfilled the following requirements: age range 18–65 years, German as native language, right-handed (criteria on the Oldfield scale 1971: 8 of 10 items positive), no history of neurological and/or medical illness or of alcohol/drug abuse, no movements disturbances caused by orthopaedic/neurological (inclusively EPMS syndromes as clinically evaluated)/surgical factors.

In all patients fulfilling the above conditions, one study physician (R.S. or L.R.) rated the psychopathology with the Brief Psychiatric Rating Scale (Overall and Gorham 1976) and the Munich version of the Scale for Assessment of Negative Symptoms (Andreasen 1981; Dieterle et al. 1986). According to ICD-9 and DSM-III criteria a study diagnosis was established, using the psychopathological status and a semistructured psychiatric interview. If the diagnosis was consistent with the preliminary clinical diagnosis, the informed consent of the patient was asked for; if obtained, the patient was included in the investigation.

A total of 179 persons were included in this study, 140 of them psychiatric patients, who can be described as follows: *schizophrenic males* ($n = 23$), average age 25.3 years (SD 4.5)/range 19–36, not treated with drugs from 1 week to never before; *schizophrenic females* ($n = 25$), average age 35.5 years (SD 11.6)/range 20–60, not treated with drugs from 1 week to never before; *endogenous depressed males* ($n = 26$), average age 41.1. (SD 11.8)/range 20–62, treated with antidepressants only; *endogenous depressed females* ($n = 37$), average age 44.4 (SD 11.8)/range 20–61, treated with antidepressants only; *non-endogenous depressed males* ($n = 11$), average age 30.0 (SD 11.5)/range 18–50, not treated with drugs from 1 week to never before; *non-endogenous depressed females* ($n = 18$), average age 30.9 (SD 10.9)/range 18–53, not treated with drugs from 1 week to never before. *Control persons* were coworkers of the hospital (physicians, nurses, labourers and medical students/relatives: *healthy males* ($n = 22$), average age 32.0 (SD 9.1)/range 20–57, no drug treatment; *healthy females* ($n = 17$), average age 34.8 (SD 14.1)/range 20–62, no drug treatment.

Since the patient groups were different in age, it was necessary to select randomly "age-matched" subgroups from the above control population for statistical comparisons.

Investigation Times

All patients were examined on the day of admission or the morning thereafter (measurement 1). All patients were to be reinvestigated after 14 days (measurement 2), and on the day before discharge (measurement 3). Unfortunately, we experienced a high number of "drop-outs" especially for measurement 3 (discharge against medical advice, transfer to another hospital, refusal of a third EEG mapping examination), which may have biased especially measurement 3. We therefore will not further statistically evaluate measurement 3, and will have to discuss the results of measurement 2 with caution.

EEG Mapping System

A commercial 16-channel EEG mapping system (Alvar Paris Cartovar C I) was used as the data basis for power values and

mapping (full details in Günther and Breitling 1985). The electrode placement (using the international 10/20 system) and the nomenclature are demonstrated in Fig. 1.

Further technical details were as follows: 16 average reference derivations; calibration 17.6 μV equalling 0.7 cm, bandpass filter 0.5–30 Hz, selective filter 50 Hz; time constant 0.3 s. The analog EEG signal was digitalized with a frequency of 68 Hz. As artefact-free 30-s periods as possible (criteria and advice J. Kugler, Munich) were selected for fast Fourier transform analysis in the frequency range of 0.5–30 Hz in steps of 1/2 Hz (yielding 60 power histograms in microvolt square). The length of EEG period selected was the same in every subject and task.

The power values were then summarized into the usual frequency bands delta 0.5–4.0 Hz, theta 4.5–7.5 Hz, alpha 8.0–13.0, beta 1 13.5–20.0 and beta 2 20.5–30.0, and used as the basis for further statistical evaluation. We did not attempt in this very large study to investigate 1/2 Hz steps, since we were forced to reduce the enormous amount of data. Additionally, we wanted to use similar frequency bands as in our previous EEG mapping studies for better comparison.

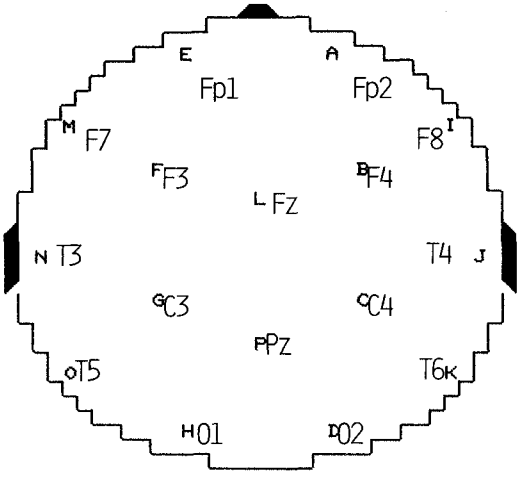


Fig. 1. Nomenclature of the 16-channel EEG mapping system (Alvar Paris C-I) and electrode placement according to the 10/20 system

Investigation Situation (Fig. 2)

The subject was seated comfortably in an EEG chair in a light-adapted, noise-protected special EEG investigation room. The eyes were closed during the relaxation period and the simple motor tasks (and music perception tasks; will be reported elsewhere). The eyes were open for a reference period and the visuomotor tasks subsequently. The ears were plugged with earphones, both to protect from remaining external noise and to provide short reminders of the instructions (and the music tasks).

The EEG was continuously monitored by 16-channel polygraph in order to avoid the inclusion of artefact-contaminated periods into the FFT analysis.

The exact schedule of the tasks was as follows.

First Part: Eyes Closed

1. Calibration period (one derivation 01–02 on all 16 channels; no differences greater than 5% in the total energy were permitted) (30 s)

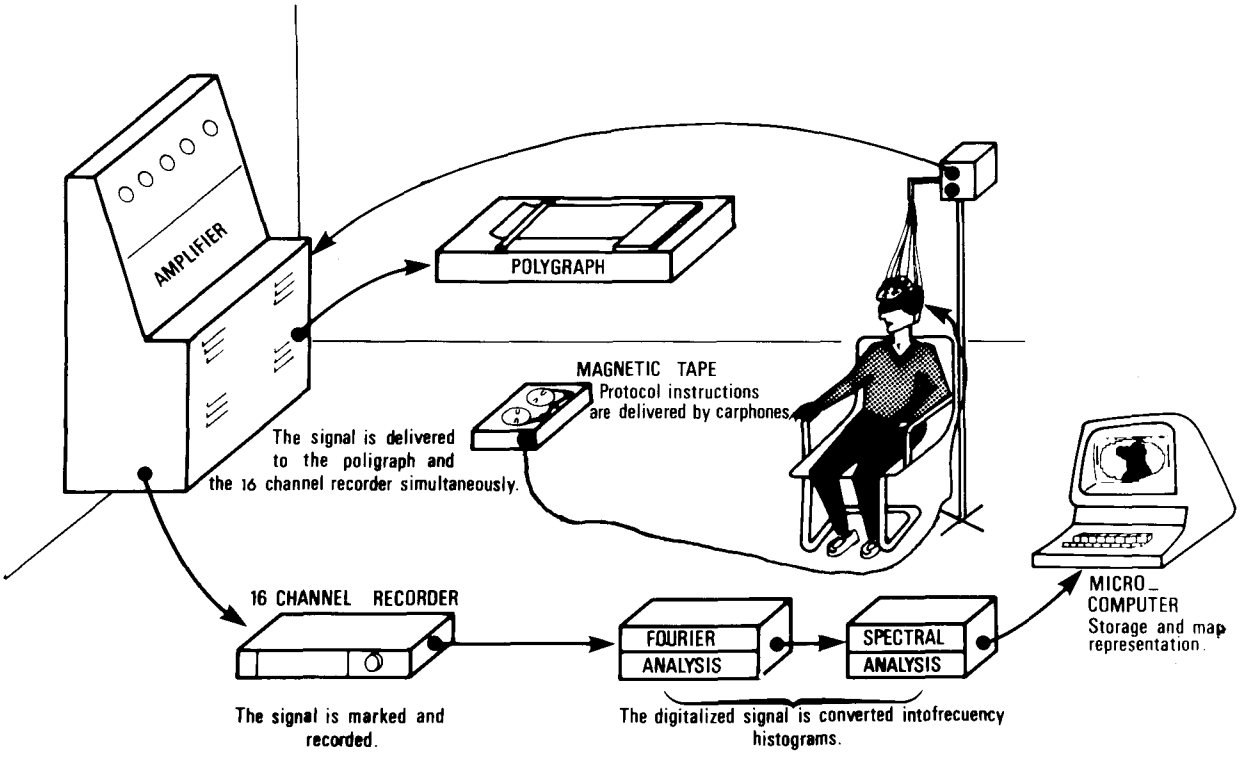


Fig. 2. Experimental situation

2. Relaxation 1: obtained after a 6-min relaxation period/autogenous training (Schultz 1960; Günther and Breitling 1985) (30s)(r1)
3. Repetitive movement right hand (fist opening and closing with a frequency of 1/s)(30s)(hr)
4. Repetitive movement left hand (30s)(hl)
(5.–8. Music perception tasks, not reported here)

Second Part: Eyes open

9. Eyes open/fixation (30s)(aa)
10. Pursuit rotor right hand (*Motorische Leistungsserie;* Schoppe 1974; Günther and Gruber 1983)(30s)(pr)
11. Pursuit rotor left hand (pl)(30s)
12. Steadiness right hand (sr)(30s)
13. Steadiness left hand (sl)(30s)
(14.–17. Music reproduction/intermittent light, not reported here)

Psychomotor Variables

The performance quality of each subject in the motor tasks was assessed using the following variables of the *Motorische Leistungsserie* (detailed descriptions in Günther und Gruber 1983; Günther et al. 1986a, 1988a).

Pursuit rotor right hand –faults 1. half (p.r.f.1.h.)
Pursuit rotor right hand –faults duration 1. half (p.r.fd.1.h.)
Pursuit rotor right hand –faults 2. half (p.r.f.2.h.)
Pursuit rotor right hand –faults duration 2. half (p.r.fd.2.h.)
Pursuit rotor right hand –faults total (p.r.ft.)
Pursuit rotor right hand –faults duration total (p.r.fd.t.).
Pursuit rotor left hand –faults 1. half (p.l.f.1.h.)
Pursuit rotor left hand –faults duration 1. half (p.l.fd.1.h.)
Pursuit rotor left hand –faults 2. half (p.l.f.2.h.)
Pursuit rotor left hand –faults duration 2. half (p.l.fd.2.h.)
Pursuit rotor left hand –faults total (p.l.ft.)
Pursuit rotor left hand –faults duration total (p.l.fd.t.).

Steadiness right hand –faults (s.r.f.)
Steadiness right hand –faults duration (s.r.fd.)
Steadiness left hand –faults (s.l.f.)
Steadiness left hand –faults duration (s.l.fd.)

Psychopathology Variables

The psychopathological status in each patient was assessed by a study physician, who was not informed of the preliminary clinical diagnosis of the patient, and was not directly involved in the EEG mapping or the statistical evaluation thereof.

We used the following variables. SANS (Munich version) (MV-SANS; Dieterle et al. 1986):

Total score	(SANS)

BPRS sum scores on the following factors:

Anxiety-depression	(ANDP1)
Anergia	(ANER1)
Thought disturbance	(THOT1)
Activation	(ACT1)
Hostility	(HOST1)

Other Variables

Besides age, sex, and preliminary clinical diagnoses, we documented the actual medication for the patient groups in which this was applicable (i.e. endogenous depressed patients at all times; all patients: measurements 2 and 3).

Results EEG Mapping

Resting Conditions Measurement 1

Statistical Procedures

We calculated "grand means", i.e. average values of power over all electrodes in each frequency band and group. They are listed in Table 1a (eyes closed and 1b (eyes open). Inspection of the tables reveals good consistency of the resting values for the various "matched" subgroups of normals.

In order to screen statistically differences in resting conditions between *patients and matched normal groups,* we calculated repetitive *t*-tests for independent samples, separately for each electrode, frequency band, and "eyes open/closed" with corrections of the alpha niveau. This procedure (Abt 1981) was selected instead of ANOVA and subsequent *t*-tests for technical reasons (too large data sets for our computer facilities). However, it is pointed out that the Bonferroni-Holm correction chosen (Abt 1981; O'Brien and Kaiser 1985) is conservative (keeping down "type I" errors, i.e. finding differences where there are none), which seems a suitable approach to our resting data.

For the group NEU (-rotic depressed patients; group characteristics have been given in the subjects section above), we found 4 *t*-values (of 160: 5 frequency bands × 16 electrodes × 2 (eyes open/closed) conditions) in males, and 5 in females which were below a P of 5%, which is less than would be expected by chance. Therefore, a correction of the alpha niveau was not necessary and the 0-hypothesis of no differences between NEU and CNT (control persons) was supported.

For SCH(izophrenic) females, there were 0 (!) significant *t*-values when comparing them with their matched normals. However, in schizophrenic males, we found 34 (of 160) *t*-values which were below $P = 5\%$, which called for correction of the alpha niveau. We performed the Bonferroni-Holm correction, and found 0 values, which were significant after correction. Since this procedure is statistically conservative (see above), we may run risks of accepting the 0-hypothesis erroneously ("type II" error) and report these differences therefore *as a tendency*.

Eyes closed: higher power values in delta (in F3); higher values in beta 1 in Fp2 (muscle artefacts?), F4, O1; higher values in beta 2 in Fp2 (artefacts?), F3, Fz. Thus, the majors differences (tendency only) concern frontal and prefrontal regions in untreated schizophrenics in resting conditions, but predominantly males.

Eyes open: higher values in delta in F4, O2, F3, O1, F8 (eye artefacts?), T4, T6, Fz, F7 (?), T3, T5, Pz; higher values in beta 1 in Fp2 (?), F4, F3, F8 (?)

Table 1a. Grand means (average over all subjects and electrodes) of power and standard deviation in all frequency bands for *resting/eyes closed* conditions

	SCHM	MSCM	SCHF	MSCF	NEDM	MNDM	NEDF	MNDF	DEPM	MDEM	DEPF	MDEF
Delta												
x	157.50	113.88	122.94	127.13	115.06	112.81	141.94	128.81	109.94	140.25	116.31	126.25
SD	(104.84)	(76.88)	(79.44)	(83.70)	(73.76)	(60.70)	(82.09)	(90.99)	(70.50)	(83.22)	(76.49)	(83.05)
Theta												
x	24.25	20.38	24.63	30.25	26.69	21.56	28.94	30.06	26.25	20.56	37.50	29.56
SD	(6.91)	(4.83)	(4.38)	(5.59)	(5.57)	(4.37)	(5.72)	(16.07)	(6.09)	(4.24)	(8.21)	(5.28)
Alpha												
x	97.94	140.75	132.38	146.50	89.94	132.81	169.31	143.94	112.75	95.25	171.81	155.50
SD	(54.89)	(72.07)	(78.59)	(71.63)	(46.60)	(64.18)	(99.50)	(70.98)	(58.94)	(42.00)	(72.72)	(65.47)
Beta 1												
x	44.50	33.06	51.38	54.50	34.38	35.00	73.81	51.31	88.56	32.25	67.38	54.94
SD	(9.32)	(7.68)	(8.86)	(12.39)	(7.70)	(8.56)	(12.05)	(12.39)	(13.83)	(6.31)	(13.40)	(11.11)
Beta 2												
x	47.06	28.81	54.81	50.19	27.13	32.94	66.50	51.63	90.69	31.63	59.13	54.75
SD	(18.82)	(8.85)	(22.95)	(19.06)	(13.06)	(9.45)	(25.97)	(21.22)	(10.95)	(9.56)	(24.00)	(25.66)

Note that there were *no* statistically significant differences between subgroups of patients and controls
Abbrevations: SCHM = Schizophrenic males; MSCM = match group to schizophrenic males; SCHF = schizophrenic females; MSCF = match group to schizophrenic females; NEDM = non-endogenous depressed males; MNDM = match group to non-endogenous depressed males; NEDF = non-endogenous depressed females; MNDF = match group to non-endogenous females; DEPM = endogenous depressed males; MDEM = match group to endogenous depressed males; DEPF = endogenous depressed females; MDEF = match group to endogenous depressed females

Table 1b. Grand means (average over all subjects and electrodes) of power and standard deviation in all frequency bands for *resting/eyes open* conditions

	SCHM	MSCM	SCHF	MSCF	NEDM	MNDM	NEDF	MNDF	DEPM	MDEM	DEPF	MDEF
Delta												
x	145.44	95.31	156.13	101.50	121.06	80.56	156.50	114.13	95.06	89.81	137.60	105.63
SD	(83.01)	(59.62)	(88.33)	(57.35)	(66.98)	(36.21)	(75.92)	(69.10)	(51.91)	(48.02)	(78.83)	(68.79)
Theta												
x	19.44	17.38	22.00	21.69	21.13	18.06	23.31	20.44	17.88	16.69	22.38	20.25
SD	(4.73)	(4.18)	(5.33)	(4.96)	(5.07)	(3.45)	(4.33)	(5.07)	(4.70)	(3.50)	(4.63)	(4.78)
Alpha												
x	45.50	50.25	49.88	70.19	43.56	50.56	65.75	52.56	50.50	45.06	80.06	68.83
SD	(10.79)	(8.64)	(11.11)	(17.04)	(12.53)	(9.51)	(15.72)	(11.40)	(12.27)	(7.41)	(17.05)	(16.05)
Beta 1												
x	37.19	25.06	49.63	55.44	30.38	30.19	72.44	51.31	34.81	28.69	68.50	55.38
SD	(8.07)	(5.71)	(16.10)	(15.77)	(8.20)	(9.07)	(19.25)	(18.11)	(5.67)	(6.98)	(15.61)	(16.13)
Beta 2												
x	49.25	25.56	73.63	64.88	38.25	37.50	82.06	66.56	43.81	32.63	75.56	66.56
SD	(21.25)	(11.95)	(41.49)	(37.25)	(24.84)	(21.63)	(62.33)	(42.64)	(17.24)	(16.35)	(44.46)	(39.59)

Note that there were *no* statistically significant differences between subgroups of patients and controls
Abbrevations as in Table 1a.

Fz; higher values in beta 2 in F4, C4, O2, F3, T6, Fz, F7 (?), Pz (thus bilateral diffuse increases in schizophrenic males).

For endogenous DEP (-ressive) males, there were 0 (!) significant *t*-values with a *P* below 5%, when their resting conditions were compared with those of their matched controls. In endogenous DEP (-ressive) females, finally, there were 2 "significant" *t*-values, which is less than expected by chance (which would be 8).

Therefore, for endogenous depressed patients (both males and females) also, there is no evidence suggesting differences to normals in resting conditions.

In conclusion, there were *no significant differences* in our eyes open/closed resting conditions between patients and controls persons.

Resting Conditions Controls Measurements 1 and 2 (Test-Retest Reliability)

In order to obtain some information on the test-retest reliability over 2 weeks we statistically screened this for the whole control group for eyes closed conditions. Since the patients received different medication on these investigations and were different in their psychopathological status, we did not undertake this for the patient groups. (However, all results on activation conditions at all times shall be detailed below.)

For normals, we found among 160 paired *t*-tests (resting measurement 1 vs 2) 0 (!) *P* values below 5%.

This strongly supports both time stability and test-retest reliability of our eyes closed EEG mapping parameters, which we consider important and which has not been reported before, to our knowledge.

Activation Conditions

Statistical Procedures

We calculated multifactorial analyses of variance for the factors *frequency bands (5) × tasks (7 "non-visual", 9 "visual") × electrodes (16),* including the interactions of first rank (higher-rank interactions contained too many 0 values in the fields calculated and had to be omitted, cf. SPSS users guide, 2nd edn, p. 464ff).

First, ANOVAs were calculated independently for the control groups, the endogenous depressive patients, the non-endogenous depressive patients and the schizophrenics (taking all subjects in each group).

Subsequently, the endogenous depressed patients were subdivided into "mild/severe" (cut-off score: median of raw score on the factor anergia/depression of the BPRS, which yielded 16 in males and 18 in females respectively). Similarly, the non-endogenous depressed patients were subdivided at their median on the factor anergia/depression, which was 12 in males and 14 in females. Finally, the schizophrenics were subdivided at their median of total raw score on

Table 2. Analyses of variance-motor activation conditions (*P* of F-values)

	Delta		Theta		Alpha		Beta 1		Beta 2	
	NV	V	NV	V	NV	V	NV	V	NV	V
Controls male										
Tasks	000	000	000	000	000	000	000	000	000	000
Electrodes	000	000	000	000	000	000	000	000	000	000
Interactions	000	000	NS	NS	NS	NS	000	000	000	000
Controls female										
Tasks	000	000	000	NS	000	000	000	001	050	000
Electrodes	000	000	000	000	000	000	000	000	000	000
Interactions	NS	000	NS	NS	NS	NS	NS	001	NS	000
Schizophrenics male sans < 71										
Tasks	000	000	000	001	000	NS	000	000	015	000
Electrodes	000	000	000	000	000	000	000	000	000	000
Interactions	NS	008	NS	NS	NS	NS	NS	NS	NS	NS
Schizophrenics male sans ≥ 71										
Tasks	000	000	001	000	000	000	019	022	NS	000
Electrodes	000	000	000	000	000	000	000	000	000	000
Interactions	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Schizophrenics female sans < 51										
Tasks	000	000	007	001	000	016	015	NS	033	NS
Electrodes	000	000	000	000	000	000	000	000	000	000
Interactions	NS	000	NS	NS	NS	NS	NS	NS	NS	NS
Schizophrenics female sans ≥ 51										
Tasks	000	000	000	NS	000	001	004	000	000	000
Electrodes	000	000	000	000	000	000	000	000	000	000
Interactions	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Non-end. depression male andp < 12										
Tasks	NS	000	NS	NS	000	000	000	000	000	001
Electrodes	000	000	000	000	000	000	000	000	000	000
Interactions	NS	000	NS	NS	NS	NS	025	NS	NS	NS
Non-end. depression male andp ≥ 12										
Tasks	000	000	004	NS	000	NS	000	000	000	000
Electrodes	000	000	020	002	000	000	000	000	000	000
Interactions	NS	000	NS	NS	NS	NS	NS	NS	NS	NS
Non-end. depression female andp < 14										
Tasks	036	000	001	003	000	000	NS	023	NS	NS
Electrodes	000	000	000	000	000	000	000	000	000	000
Interactions	NS	000	NS	NS	NS	NS	NS	NS	NS	NS
Non-end. depression female andp ≥ 14										
Tasks	000	000	000	000	000	000	NS	000	033	000
Electrodes	000	000	000	000	000	000	000	000	000	000
Interactions	NS	000	NS	NS	NS	NS	NS	NS	NS	NS
Endogen. depression male andp < 16										
Tasks	000	000	000	NS	000	000	000	000	000	000
Electrodes	000	000	000	000	000	000	NS	000	NS	000
Interactions	NS	000	NS	NS	NS	NS	NS	NS	NS	NS
Endogen. depression male andp ≥ 16										
Tasks	000	000	000	050	000	000	000	000	020	000
Electrodes	000	000	000	000	000	000	000	000	000	000
Interactions	NS	061	NS	NS	NS	NS	NS	NS	NS	NS
Endogen. depression female andp < 18										
Tasks	000	000	000	000	000	000	000	000	044	000
Electrodes	000	000	000	000	000	000	000	000	000	000
Interactions	000	000	NS	NS	NS	NS	NS	NS	047	NS

Table 2 (continued)

	Delta		Theta		Alpha		Beta 1		Beta 2	
	NV	V	NV	V	NV	V	NV	V	NV	V
Endogen. depression female andp ≥ 18										
Tasks	000	000	000	000	000	000	NS	000	NS	000
Electrodes	000	000	000	000	000	000	000	000	000	000
Interactions	004	000	NS	NS	NS	NS	NS	NS	NS	000

Multiple analyses of variance for the factors frequency bands (5) × tasks (7 NV = non-visual, 9 V = visual) × electrodes (16) were performed independently for all groups. Note significant F values in all groups and frequencies for the factors tasks and electrodes. Note several significant task × electrodes interactions.

Abbrevations: sans = scale for assessment of negative symptoms, andp = anergia/depression scale. Non-end. = non-endogenous, endogen. = endogenous.

the SANS-indicating "negative symptoms", yielding 71 in males and 51 in females.

This statistical procedure is analogous to that used in our previous EEG mapping studies on neuroleptic-treated schizophrenics (detailed in Günther and Breitling 1985). Table 2 shows the probabilities for the F-values calculated in various ANOVAs. As can be seen from this table, there were significant F-values in *all* frequency bands, in *all* task conditions and electrodes. Additionally, there were at least several significant first rank (i.e. task × electrode) interactions, which suggests that a subsequent *t*-test analysis should be calculated separately for each task *and* each electrode (cf. Günther and Breitling 1985, p. 519ff).

Detailed statistical tables and/or maps are given in some frequency bands only for the simple motor tasks and subgroups of patients for space reasons; the other information is provided in general outline.

Delta Frequency Band (0.5–4.5 Hz)

Simple Motor Activation Measurement 1

The significant changes (P below 0.05 as compared with resting conditions) in different patient groups are listed in Table 3a.

Male Persons: lines 1–7

Line 1 shows EEG results in male schizophrenics (SCH-M; $n = 23$, average age 25.3 years, range 19–36), as compared with their matched control group (MSC-M; $n = 17$; average age 28.2 years, range 20–36). As can be seen, there are more significant increases in schizophrenics (23 vs 4), even more markedly seen in left hand movement. This differences 23 vs. 4 is, of course, significant on statistical screening (e.g. chi-square 23.16, $df = 1$, $P < 0.001$).

Line 2 shows the results in male endogenous depressed patients (DEP-M; $n = 26$, 41.1/20–62); matched control group MDE-M, $n = 13$; average age 34.1, range 20–57. There are no differences between the groups on statistical screening.

Line 3 shows the male non-endogenous depressed patients (NED-M; $n = 11$; age 33.8/18–50) and the matched control group (MND-M; $n = 10$; age 34.3/20–57). There are more increases in patients than controls (16 vs 4; chi-square 7.74, $df = 1$, $P < 0.01$). This difference is predominantly during left hand movement.

If one separates the psychotic patients at their median, detailed above in the statistical procedures, the following results in this frequency band are obtained.

Line 4: male schizophrenics below median on the negative symptomatology (SANS 71) (SCB-M; $n = 12$; age 25.5/21–36) and their matched control group (MSB-M; $n = 10$, age 26.6/20–36): no difference.

Line 5: male schizophrenics above median (SCA-M; $n = 11$; 25.1/19–35) versus control group MSA-M ($n = 9$; 26.8/20–36): signs of overactivation in patients (25 increases vs 10, chi-square 14.18, $P < 0.001$), which is more marked on left hand task.

Lines 6 and 7: male endogenous depressed patients below and above median (raw score on the factor ANDP of the BPRS) (below: DEB-M, $n = 13$, 40.5/20–58, control group MDB-M, $n = 8$, 36.8/20–57; above: DEA-M, $n = 19$, 38.2/29–61, control group MDA-M, $n = 9$, 37.6/20–57): no differences.

Female Persons: Lines 8–14

Line 8: Female schizophrenics (SCH–F; $n = 25$, 35.5/20–60), as compared with matched controls (MSC-F; $n = 16$, 33.1/20–61). Similarly to male schizophrenics there are signs of hyperactivation (14 vs 4 increases, chi-square 7.76, $df = 1$, $P < 0.01$), predominantly in left hand movement.

Line 9: female endogenous depressed patients (DEP-F; $n = 37$, 44.4/20–61) and their matched control group (MDE-F; $n = 15$; 36.5/20–62): no differences.

Line 10: female non-endogenous depressed patients (NED-F; $n = 18$; 30.9/18–53) and their matched control group (MND-F; $n = 13$ 30.3/20–53): no differences.

Line 11: female schizophrenic patients below median (51 on the SANS) (SCB-F; $n = 13$, 35.5/20–60) and the matched control group (MSB-F; $n = 9$, 34.3/20–61): signs of hyperactivation (7 vs 0; chi-square 7.86, $df = 1$, $P < 0.01$), predominantly seen in left hand movement.

Line 12: female schizophrenic patients above median (SCA-F; $n = 12$, 35.5/20–60), controls MSA-F ($n = 11$, 34.3/20–52): no differences.

Table 3. Activation patterns in different patients subgroups during repetitive movement with the right hand (left half) and left hand (right half). Table 3a. Delta frequency band (0.5–4.0 Hz). Table 3b. Alpha frequency band (8.0–13.0 Hz). Table 3c. Beta 1 frequency band (13.5–20.0 Hz)

		Repetitive fist opening right hand (Electrode position)															Repetitive fist opening left hand (Electrode position)														
		left							central		right						left							central		right					
		Fp1	F3	C3	O1	F7	T3	T5	Fz	Pz	Fp2	F4	C4	O2	F8	T4	T6	Fp1	F3	C3	O1	F7	T3	T5	Fz	Pz	Fp2	F4	C4	O2	F8	T4	T6
		E	F	G	H	M	N	O	L	P	A	B	C	D	I	J	K	E	F	G	H	M	N	O	L	P	A	B	C	D	I	J	K
a)	1. Measurement/delta. Males lines 1–7																															
1	SCH-M	+	+			+			+		+	+		+	+			+	+	+	+	+	+	+	+	+	+	+	+	+		+
	MSC-M	+									+							+									+						
2	DEP-M	+									+		−					+	−														
	MDE-M	+																+															
3	NED-M	+					+				+	+						+	+		+	+	+		+	+	+	+	+	+	+		
	MND-M	+									+								+									+					
4	SCB-M																										+						
	MSB-M	+									+							+									+						
5	SCA-M	+	+			+	+				+	+			+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
	MSA-M	+								+	+			+				+			+			+	+		+	+					
6	DEB-M																																
	MDB-M	+				−												+									+						
7	DEA-M	+		−	−						+							+									+						
	MDA-M	+									+							+									+						
Females lines 8–14																																	
8	SCH-F	+									+	+						+	+			+	+	+			+	+		+	+	+	+
	MSC-F	+									+							+									+						
9	DEP-F	+	+	−							+	+						+	+								+						
	MDE-F	+									+							+									+						
10	NED-F																	+									+						
	MND-F	+									+							+									+						
11	SCB-F									+												+	+			+					+	+	+
	MSB-F																																
12	SCA-F	+	+								+	+						+	+					+			+	+					
	MSA-F	+							+		+	+					+	+							+		+				+		
13	DEB-F	+	+						+		+	+						+									+	+					
	MDB-F	+									+							+															
14	DEA-F	+		−																−													
	MDA-F	+																															
b)	1. Measurement/alpha. Males lines 1–7																															
1	SCH-M												−					−															
	MSC-M	−		−		−	−				−		−			−				−	+								−	+			

Table 3. Activation patterns in different patients subgroups during repetitive movement with the right hand (left half) and left hand (right half). Table 3a. Delta frequency band (0.5–4.0 Hz). Table 3b. Alpha frequency band (8.0–13.0 Hz). Table 3c. Beta 1 frequency band (13.5–20.0 Hz)

		Repetitive fist opening right hand (Electrode position)															Repetitive fist opening left hand (Electrode position)													
		left							central		right						left							central		right					
		Fp1 E	F3 F	C3 G	O1 H	F7 M	T3 N	T5 O	Fz L	Pz P	Fp2 A	F4 B	C4 C	O2 D	F8 I	T4 J	T6 K	Fp1 E	F3 F	C3 G	O1 H	F7 M	T3 N	T5 O	Fz L	Pz P	Fp2 A	F4 B	C4 C	O2 D	F8 I	T4 J	T6 K
2	DEP-M	–		–		–	–			–			–		–																
	MDE-M																														
3	NED-M		–	–			–	–	–			–	–			–	–		–	–				–				–			
	MND-M																														
4	SCB-M												–																		
	MSB-M																												+		
5	SCA-M													+				–		–											
	MSA-M			–		–																									
6	DEB-M			–												–															
	MDB-M																														
7	DEA-M				+	–								–							+								+		
	MDA-M															–															
Females lines 8–14																															
8	SCH-F	–	–	–					–	–	–	–	–				–	–			+					–					
	MSC-F			–		–							–																		
9	DEP-F	–		–						–	–			+			–									–			–	+	
	MDE-F			–		–							–	–																	
10	NED-F			–				–		–			–			–															
	MND-F		–	–		–			–				–						–	–									–		
11	SCB-F																				+										
	MSB-F			–				–					–																		
12	SCA-F	–	–	–					–	–	–						–	–			+					–					
	MSA-F			–				–												–											
13	DEB-F																								–						
	MDB-F			–									–																		
14	DEA-F			–				–					–	+		–				–	+								+		
	MDA-F			–																											
c) 1. Measurement/beta 1. Males 1–7																															
1	SCH-M		–	–				–										–							–						
	MSC-M	–	–	–		–			–	–	–	–	–		–			–	–						–	–			–			–
2	DEP-M																														
	MDE-M	–	–	–					–	–			–			+		–	–										+		
3	NED-M			–				–		–							–									–					–
	MND-M		–	–					–	–			–			+				–											

4	SCB-M	−	−	−				−			−	−	−					−	−	−					−								
	MSB-M		−																										−	+		−	
5	SCA-M																																
	MSA-M		−						−	−			−																−	+			
6	DEB-M																																
	MDB-M			−									−							−	+												
7	DEA-M		−	−					−																								
	MDA-M	−	−	−		−			−	−			−							−	+												
Females lines 8–14																																	
8	SCH-F	−	−	−		−			−	−		−	−		−			−		−					−	−			−				−
	MSC-F	−	−	−					−	−		−	−																−				
9	DEP-F	−	−	−				−	−	−	−	−	−		−			−	−	−		−			−	−			−				−
	MDE-F	−	−	−		−		−	−	−		−	−		−		−												−				
10	NED-F			−					−				−		−										−				−				
	MND-F	−	−	−		−		−	−	−		−	−		−				−	−		−	+		−	−	−		−		−		
11	SCB-F		−	−					−	−	−	−	−					−				−			−								
	MSB-F	−	−	−					−				−				−																
12	SCA-F	−	−	−		−			−	−			−					−											−				
	MSA-F	−	−	−				−	−	−	−		−		−				−	−					−	−	−		−				
13	DEB-F		−	−				−	−	−		−	−		−				−	−					−	−			−				−
	MDB-F	−	−	−		−		−	−	−	−	−	−		−		−												−				
14	DEA-F		−	−					−										−	−					−				−				
	MDA-F	−	−	−					−				−						+	+					+				+				

Only significant (P below 0.05) increases (+) or decreases (−) in power (evaluated by analyses of variance and t-test, in comparison to resting conditions) are demonstrated for the following populations: SCH-M, schizophrenic males (detailed group descriptions in "Methods" section); MSC-M, match group to schizophrenic males; DEP-M, depressive (endogenous) males; MDE-M, match group to depressive (endogenous) males; NED-M, non-endogenous depressed males; MND-M, match group to non-endogenous depressed males; SCB-M, schizophrenics below median of negative symptoms-males; MSB-M, match group to schizophrenics below median-males; SCA-M, schizophrenics above median-males; MSA-M, match group to schizophrenics above median-males; DEB-M, depressive (endogenous) below median of depressive symptoms-males; MDB-M, match group to depressives (endogenous) below median-males; DEA-M, depressives (endogenous) above median-males; MDA-M, match group to depressives above median-males; SCH-F, schizophrenic females; MSC-F, match group to schizophrenic females; DEP-F, depressive (endogenous) females; MDE-F, match group to depressive (endogenous) females; NED-F, non-endogenous depressed females; MND-F, match group to non-endogenous depressed females; SCB-F, schizophrenics below median of negative symptoms-females; MSB-F, match group to schizophrenics below median-females; SCA-F, schizophrenics above median-females; MSA-F, match group to schizophrenics above median females; DEB-F, depressives (endogenous) below median of depressive symptoms-females; MDB-F, match group to depressives (endogenous) below median-females; DEA-F, depressives (endogenous) above median-females; MDA-F, match group to depressives above median-females.

Note that most differences between patients and control persons are found in delta frequency band, and less in alpha and beta 1 bands (differences in the theta and beta 2 bands not demonstrated are even smaller). Details are discussed (for space reasons) in the "Results" section only.

Line 13: female endogenous depressed patients below median (18 on the factor ANDP of the BPRS) (DEB-F; $n = 18$, 40.4/20–58) and their matched control group (MDB-F; $n = 14$, 37.5/20–62): no differences (8 vs 3, chi-square 2.76, NS).

Line 14: female endogenous depressed patients above median (DEA-F; $n = 19$, 48.2/29–61), as compared with matched controls MDA-F ($n = 9$, 45.3, 30–62): no differences.

Visuomotor Activation Measurement 1 and 2

In the delta frequency band, we obtained for all groups, i.e. psychiatric patients and control persons, very widespread (involving almost all electrodes) EEG activation patterns, without evidence of differences between groups. This will not be detailed further, taking into account additionally that there were serious and inevitable artefact problems (eye movements for controlling the visuomotors tasks).

Simple Motor Activation Measurement 2

The marked changes for one subgroup of patients (male schizophrenics and their control group) along with psychopathological improvement (BPRS total score from 54.2/measurement 1, to 25.6/measurement 2) are demonstrated in Fig. 3. Note the impressive reduction of the bilateral hyperactivation in schizophrenics. This applies also for schizophrenic females (and also for music reception tasks, which will be reported later). No such reduction was seen in the visuomotor tasks (probably due to artefacts which remained unchanged), nor in other patient groups from measurement 1 to 2.

It has to be pointed out that the reduction of overactivation (i.e. delta increases!) in schizophrenics is predominantly seen in patients above median, who already show this reduction excessively after 14 days of treatment. The EEG activation pattern in normal persons in delta frequency band remained stable from measurements 1 to 2 for the motor activation conditions, which points out the encouraging test-retest reliability of this examination (which is a necessary precondition for all other attempts at "external" validation of the EEG with other neuroimaging methods; e.g. Günther et al. 1988c).

Theta Frequency Band (5–7.5 Hz)

Since there were virtually no significant F-values for the interaction electrode × task in no patient subgroup (nor in normals), we had no statistical basis for further detailed analysis. This finding is congruent with the results of only minimal EEG activation in this frequency band, which we have published before (Günther and Breitling 1985; Günther et al. 1986b, 1988b).

Alpha Frequency Band (8.0–13.0)

Simple Motor Activation Measurement 1

The significant changes in the various group are shown in Table 3b. Inspection of the whole table reveals that major differences between patients and control persons are predominant in right hand movement, which will be detailed as follows.

Male Persons: Lines 1–7

Line 1 shows the results in male schizophrenics and their matched control group (group description and abbreviations as in delta frequency band, see above and Table 3), yielding signs of reduced alpha blockage in patients (2 vs 9 decreases, 0 vs 2 increases, chi-square 8.04, $df = 2$, $P < 0.05$).

Line 2 shows the results in male endogenous depressed patients and their control group, yielding more signs of alpha blockage in patients (7 vs 0 descreases (chi-square 7.86, $df = 1$, $P < 0.01$).

Line 3 shows more alpha blockage in the non-endogenous depressed patients (13 vs 0, chi-square 16.31, $df = 1$, $P < 0.001$).

Lines 4 and 5 show that the reduced alpha blockage in male schizophrenics is predominantly due to the patients above the median of negative symptomatology.

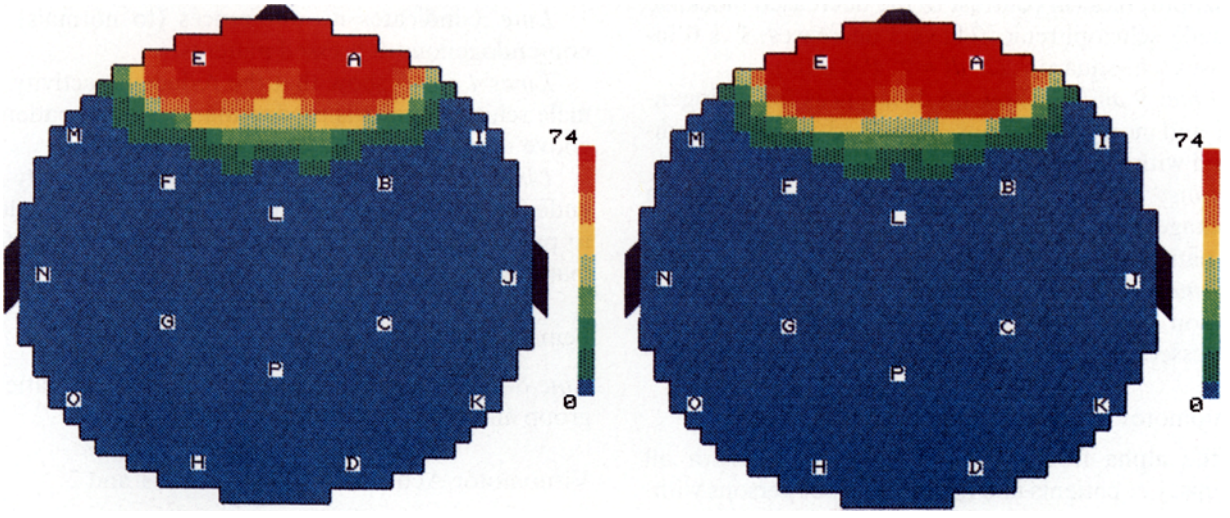
Lines 6 and 7 show that the increased alpha blockage in endogenous depressed patients is predomiantly due to patients below the median of depressive symptomatology.

Fig. 3. Statistical maps, delta (0.5–4.0 U_2) band. Left half of the whole figure: repetitive movement with the left hand, right half with the (dominant) right hand. Upper line normal males ($n = 22$), medium line male schizophrenics (not/never) drug treated; $n = 23$), lower line 16 of the above 23 schizophrenics when investigated after installation of neuroleptic treatment and psychopathological improvement. Only electrodes which change their power values in this frequency band significantly (analyses of variance and subsequent *t*-test; *P* below 0.05) as compared with resting conditions ("each subject serves as his own control") is assigned a value (of percent change) in the colour scale, which for better visual comparison is the same in all the group. The electrodes which do not change significantly remain blue. Note the bifrontal (*cave*: influences of eye movements cannot be ruled out!) "activation" in normals (*upper line*), which is contrasted by the massive "bilateral hyperactivation" in the acute, non-drug-treated schizophrenics (medium). This pattern seems to be "normalized" by neuroleptic treatment and/or psychopathological improvement (*lower line*)

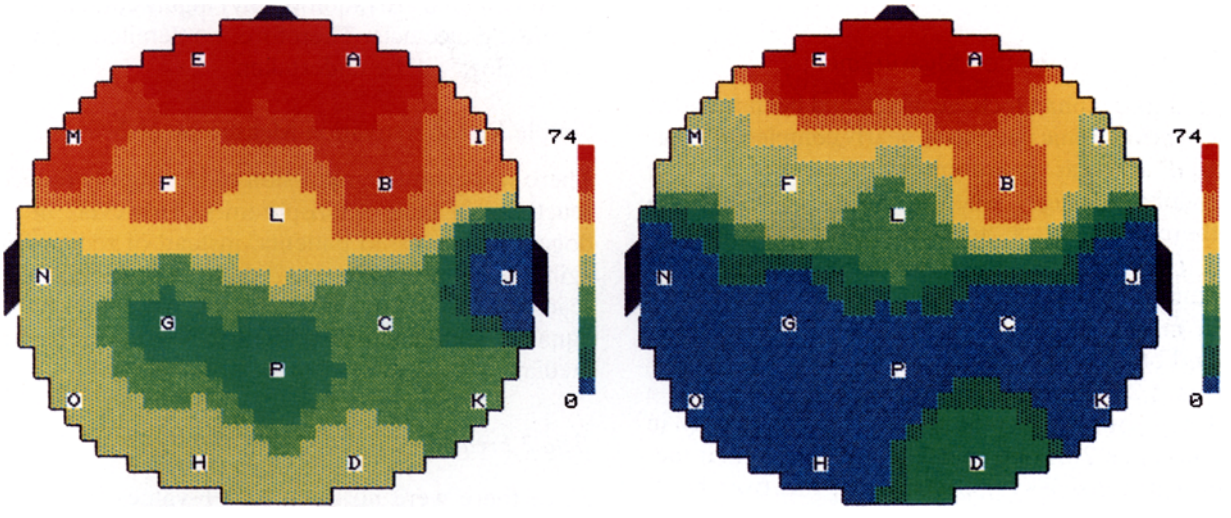
DELTA REPETITIVE MOVEMENT

LEFT HAND SIGN. INCR. IN REL.% (Vs. RESTING COND.) RIGHT HAND

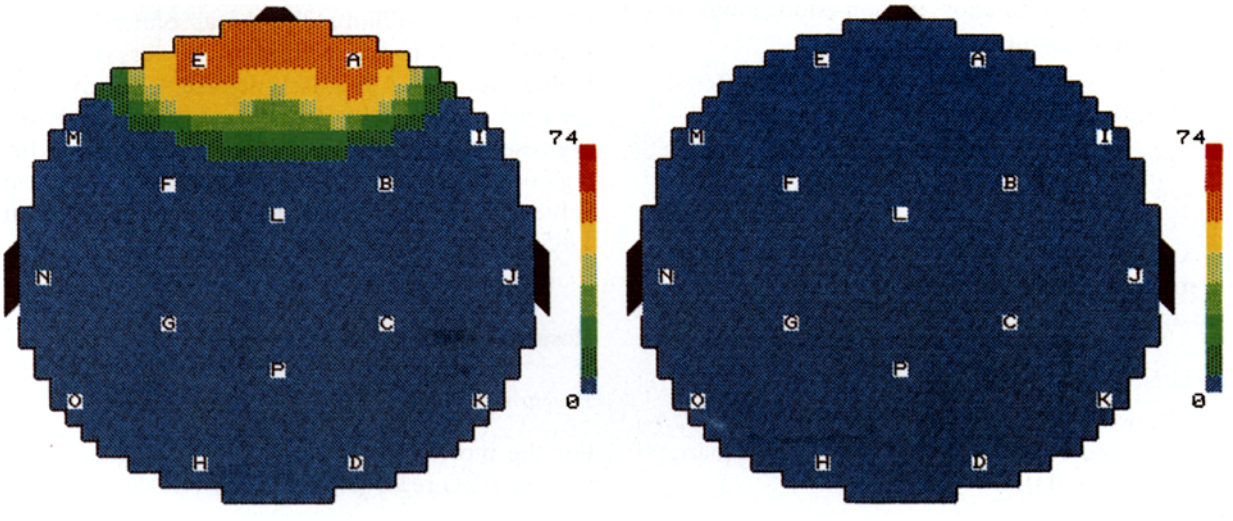
Male control persons N=22



Schizophrenics. Not/never treated with drugs before N=23



Schizophrenics. Neuroleptic-treated less than 10 days N=16



Female Persons: Lines 8–14

Line 8 shows increased alpha blockage in female schizophrenics (in contrast to the decreased blockage in male schizophrenics) (11 vs 3 decreases, 1 vs 0 increases, chi-square 7.22, $df = 2$, $P < 0.05$).

Lines 9 and 10 show no differences for endogenous and non-endogenous depressed patients, compared with healthy control persons.

Lines 11 and 12 show that the increased alpha blockage in schizophrenics is predominantly due to the patients above median.

Lines 13 and 14 confirm that no differences in activation patterns exist in subgroups of endogenous depressed patients.

Visuomotor Activation Measurement 1 and 2

In the alpha frequency band, we obtained for all groups, i.e. patients and healthy control persons without differences, very widespread alpha decreases for all visuomotor tasks. It is therefore not necessary to provide further details.

Simple Motor Activation Measurement 2

The reduced alpha blockage which had been found in male schizophrenic patients is nearly completely "normalized" towards measurement 2 (i.e. they increase their alpha blockage), whereas in female schizophrenics there is as well a "tendency towards normalization" (i.e. they decrease their overshooting alpha blockage).

In male endogenous depressed patients, the increased blockage of alpha reduces to normal in measurement 2. However, in female patients there is a tendency towards increased alpha blockage only in measurement 2. If one splits the patients at their median of depressive symptomatology, this overshooting alpha blockage is predominantly due to patients below the median. No major differences in this frequency band are obtained in non-endogenous depressed patients in measurement 2.

Beta 1 Frequency Band (13.5–20.0 Hz)

The significant changes in the various groups are shown in Table 3c. As can be seen, the changes are nearly exclusively decreases (Günther and Breitling 1985; Günther et al. 1986b, 1988b), which are somewhat more prominent on right hand movement (and which are not explained by muscle artefacts).

Male Persons: Lines 1–7

Line 1 shows reduced beta reduction in male schizophrenics (5 decreases vs 16 in controls, chi-square = 8.57, $df = 1$, $P < 0.01$).

Line 2 shows similar "non-reactivity" in endogenous depressed patients (0 vs 8 decreases, 0 vs 2 increases, chi-square = 11.86, $df = 2$, $P < 0.001$).

Line 3 indicates no differences (to normals) in non-endogenous depressed patients.

Lines 4 and 5 show that the reduced reactivity in male schizophrenics is predominantly due to patients above the median of negative syptomatology.

Lines 6 and 7 indicate that reduced reactivity in endogenous depressed patients is predominantly due to patients below the median of depressive symptomatology.

Female Persons: Lines 8–14

Line 8–14 show no differences between any patient group and their matched control groups.

Visuomotor Activation Measurement 1 and 2

In these task conditions, we obtained diffuse bilateral *in*creases that were similar in patients and control persons, which are (additionally) highly contaminated by muscle artefacts. Therefore, no detailed report of the findings will be undertaken.

Simple Motor Activation Measurement 2

There was complete remission of the slightly reduced reactivity in male schizophrenics. However, in endogenous depressed patients, instead of reduced reagibility in measurement 2 there was an increased reactivity, predominantly in female patients, which is equally found in female patients below and above the median.

Beta 2 Frequency Band (20.5–30.0 Hz)

Since there were no significant F-values for the interaction electrode × task in any group (neither patients nor controls), we had no basis for further statistical analysis. Additionally, the absolute differences resting versus task conditions were very small, and highly susceptible to muscle artefacts. For these reasons we refrained from further detailed analysis of the results. This is congruent with our previous findings of only minimal discriminant and/or functional value of this frequency band (Günther and Breitling 1985; Günther et al. 1986b, 1988b).

Results for Other Variables

Psychomotor Variables Control Persons

For the motor performance variables (under simultaneous EEG recording conditions, i.e. under "stress"

conditions) we found unexpected sex differences: females performed worse in the (spatial-motor) task pursuit rotor with both hands ($P < 5\%$/*t*-tests for independent samples for all variables mentioned):

Pursuit rotor right hand faults duration 1. half: 9.66 (SD 3.00) s versus 7.75 (2.42) in males
Pursuit rotor right hand faults duration 2. half: 9.32 (3.01) vs 6.66 (2.13)
Pursuit rotor left hand faults duration 1. half: 10.5 (3.11) vs 7.98 (2.64)
Pursuit rotor left hand faults duration 2. half: 9.83 (4.13) vs 7.58 (2.79).

Since we were not aware of findings on such motor performance sex differences in the literature (e.g. Sturm and Büssing 1985) and as the performance in females was distinctly below the normal values reported by Hamster (1980), we investigated another group of 10 females under EEG mapping conditions, in order to exclude the possibility of a biased sample. However, we obtained analogous results, which seems to suggest that *under stress conditions* (EEG mapping recording) there may be impaired motor performance in healthy females, as compared with males, in some spatial-motor tasks.

However, this preliminary finding has to be reinvestigated in a larger sample under stress and no-stress conditions (ongoing), in order to obtain further information on this possibly important issue.

Psychomotor Variables Psychiatric Patients

Since the female controls showed motor performance impairments, which have to be investigated further, we could not establish major differences from our endogenous psychotic patient groups. Therefore, we shall report in detail the motor performance results for men only.

In schizophrenic patients (males) we re-established our previous (parts I and II of this series) evidence of a "psychotic motor syndrome" (PMS) for "stress conditions" (simultanous EEG mapping) (only measurement 1 for *un*treated patients reported). In 6 of 12 pursuit rotor variables and 2 of 4 steadiness variables there were significantly ($P < 5\%$; *t*-test for independent samples) impaired performance values in patients.

For endogenous depressed patients, again, we re-established our previous findings (parts I and III of this series) of a PMS (only measurement 1 reported; *cave*: patients were treated with antidepressant medication which, however, had no influence on the PMS in our previous studies): 4 of 12 pursuit rotor variables and 2 of 4 steadiness variables were worse in patients.

In non-endogenous depressed patients such a PMS does not exist (similar to our previous results in parts I and III): O (!) of the 16 motor variables measured was different from normals. It should be noted that the ratings of depressive symptomatology were not significantly different in non-endogenous and endogenous depressed patients [13.70 (SD 5.4) vs 16.69 (SD 4.82) in the ANDP scores] and are unlikely to be responsible for the differences in motor performance.

Discussion

Our EEG mapping study on 140 psychiatric patients and 39 healthy control persons yielded results that may be of some interest for further EEG mapping studies in general and for the further exploration of brain dysfunction in psychotic patients in particular.

We confine ourselves in this paper to reporting and discussing signs of brain dysfunction, obtained during motor performance, and shall report our findings on music listening tasks separately.

First it has to be pointed out that our EEG mapping results in normal persons gave stable test-retest results both for resting conditions and motor activation states. This supports the possible usefulness of this method to explore brain function, as it may be indicated by EEG parameters in normals.

However, in *patients* who show partially grossly different EEG activation patterns, much more information will be needed for the following reasons. First, although there were considerable efforts to exclude artefact-contaminated EEG periods from further statistical evaluation, this is not entirely possible. Viewing the fact, that some schizophrenics have higher eye-blink rates than normal persons (e.g. Karson et al. 1982), this already may have influenced the findings. Secondly, there may be different "coupling" of EEG parameters to underlying brain function, as reflected, for example, by regional cerebral blood flow and glucose/oxygen consumption of parenchymal cells, which is the subject of our own ongoing positron emission tomography study (first results in Günther et al. 1988c).

Further methodological discussion of EEG mapping studies along with some of their principal problems and limitations have been provided in our previous papers (Günther and Breitling 1985; Günther et al. 1986b, 1988b) and shall be further detailed in our parallel publication on music function.

However, with the necessary caution viewing results obtained with new "imaging methods", the following statements concerning brain dysfunction in some psychiatric patient groups seem to be supported.

We re-established motor symptoms in schizophrenic and endogenous depressed patients, which were not found in non-endogenous depressed patients (irrespective of the severity of depressive symptoms), or in healthy control persons. However, owing to unexpected impaired performance in female control persons under "stress conditions", this applies for male patients only and has to be further studied in females.

In visuomotor motor activity there are severe artefact problems prohibiting further discussion. These tasks will be taken out in later studies.

During simple motor activity, all patient groups showed alteration of EEG mapping parameters during simple motor activation which were different to normal persons. Differences were maximal in schizophrenic and endogenous depressed patients, and smaller in non-endogenous depressed patients. Again, unexpected sex differences were found, which may be consistent with similar EEG mapping results during resting and cognitive activation reported recently by Petsche et al. (1988). This issue clearly needs further study in view of its general importance (for review of sex differences in brain function see, for example, Springer and Deutsch 1984, 1987).

Our EEG results on motor activation can be summarized as follows. EEG differences are predominant in the *delta frequency band.* The schizophrenic patients show a bilateral diffuse hyper"activation", which shows a tendency towards "normalization" after neuroleptic treatment and psychopathological improvement. Endogenous depressed patients show such hyperactivation to a much smaller extent, especially in female patients; no changes were seen on psychopathological improvement. Even less evidence of hyperactivation was obtained in non-endogenous patients.

In the *alpha frequency band,* most of the changes are in right hand movement, as compared with left hand movement ("greater signature"). Again the schizophrenic patients show the greatest differences to normals: reduced alpha blockage, which is not seen in other patient groups, in schizophrenics males, but increased such blockage in females. Both patterns tend to "normalize" under neuroleptic medication and improvement. Endogenous depressed patients show some minor signs of increased alpha blockage; non-endogenous and normal persons are not different.

In the *beta 1 frequency band,* again, there are differences from normals only in the schizophrenic and endogenous depressed patients, which are not present in non-endogenous depressed persons.

In conclusion we obtain by our EEG mapping parameters various signs of "pathological" motor activation patterns in schizophrenic and endogenous depressed patients, as compared with healthy control persons. Such signs are much less in non-endogenous depressed patients, however depressed they are. One might speculate that there is some "unspecific" brain dysfunction, seen possibly in many hospitalized psychiatric patients under stressful examination conditions (anxiety?, arousal?). However, this does *not* result in motor performance deficits (e.g. in non-endogenous depressed patients, as shown to be consistent with our previous findings in parts I-III). Even the more marked brain function abnormalities in schizophrenic and endogenous depressed patients do not yield motor deficits in very simple tasks. However, on more complex ones, when normal control persons "increase brain activation", no such adequate increase may be possible in patients with "longer-lasting" (and finally "structurally fixed") brain function abnormalities known especially in schizophrenic patients.

Intensive efforts will be necessary to evaluate further these speculative conclusions, involving long-term follow up investigations with EEG mapping and simultaneous MRI measurements. Both are innocuous methods allowing multiple investigations on the same persons.

In our opinion, such long-term brain function monitoring could also be of direct therapeutic value, for the following reasons. Although neuroleptics seem to "normalize" brain dysfunction in acutely psychotic "type I" schizophrenia (e.g. this paper), in a longer-lasting "brain function monitoring" signs of left hemisphere hypofunction may indeed appear later (and signs of right hemisphere overactivation, which have been described by several other authors before: Flor-Henry et al. 1979; Gruzelier 1985; Gaebel et al. 1987; Oepen and Botsch 1988).

However, speculatively, if a "compensatory overactivation" of large brain areas "burns out" ("type II"), there should be signs of "bilateral non-reactivity", which were found both in our previous EEG mapping (Günther et al. 1988b; neuroleptic-treated patients) and rCBF (Günther et al. 1986c; non-treated patients who were not acutely psychotic exacerbated) investigations.

Since neuroleptic treatment may not help much in cases of negative symptomatology ("hyporeactivity of brain function"), activating therapies should be additionally used with special advantage.

Even in "type I" schizophrenics and endogenous depressed patients, there seems to be a "lack of lateralization"/diffuse hyperactivation pattern, which might be positively aproached by "order-enhancing" therapies of different kinds (gymnastic therapy, social training, working/ergotherapy, day-hospital etc).

We have developed motor training programs for these patients and shall report some encouraging data in the last experimental report of this series.

Acknowledgements. We thank von Heyden Pharmaceuticals, Munich, for supporting the print of the colour plate.

References

Abt K (1981) Problems of repetitive significance testing. Contr Clin Trials 1:377–381

Andreasen NC (1981) Scale for the assessment of negative symptoms (SANS). The University of Iowa, Iowa

Brodie JD, Christman DR, Corona JF (1984) Patterns of metabolic activity in the treatment of schizophrenia. Ann Neurol 15 [Suppl]:S166–S169

Crow TJ (1985) The two-syndrome concept. Origins and current status. Schizophr Bull 11:471–486

Dieterle DM, Albus MI, Eben E, Ackenheil M, Rockstroh W (1986) Preliminary experiences and results with the Munich version of the Andreasen scale for the assessment of negative symptoms. Pharmacopsychiatry 19:96–100

Flor-Henry P, Koles ZJ, Howarth BG, Burton L (1979) Neurophysiology studies of schizophrenia, mania, and depression. In: Gruzelier J, Flor-Henry P (eds) Hemisphere asymmetries of function in psychopathology. Elsevier, Amsterdam, pp 481–521

Flor-Henry P, Koles ZJ, Lind J (1987) Statistical EEG investigations of the endogenous psychoses: power and coherence. In: Takahashi R, Flor-Henry P, Gruzelier J, Niwa S (eds) Cerebral dynamics, laterality and psychopathology. Elsevier, Amsterdam, pp 93–104

Gaebel W, Ulrich G (1987) Visuomotor performance and alpha-power topography in the EEG: syndrome relationships in schizophrenia. In: Takahashi R, Flor-Henry P, Gruzelier J, Niwa S (eds) Cerebral dynamics, laterality and psychopathology. Elsevier, Amsterdam, pp. 161–172

Gruzelier JH (1985) Schizophrenia. Central nervous system signs in schizophrenia. In: Vinken PJ, Bruyn GW, Klawans HL (eds) Handbook of clinical neurology, vol 2. Elsevier, Amsterdam, pp 481–521

Günther W, Breitling D (1985) Predominant sensorimotor area left hemisphere dysfunction in schizophrenia measured by brain electrical activity mapping. Biol Psychiatry 20:515–532

Günther W, Gruber H (1983) Psychomotorische Störungen bei psychiatrischen Patienten als mögliche Grundlage neuer Ansätze in Differentialdiagnose und Therapie. I. Ergebnisse erster Untersuchungen an depressiven and schizophrenen Kranken. Arch Psychiatr Nervenkr 233:187–209

Günther W, Günther R, Eich FX, Eben E (1986a) II. Cross validation study on schizophrenic patients: persistance of a "psychotic motor syndrome" as possible evidence of an independent biological marker syndrome for schizophrenia. Eur Arch Psychiatr Neurol Sci 235:301–308

Günther W, Breitling D, Banquet JP, Marcie P, Rondot P (1986b) EEG mapping of left hemisphere dysfunction during motor performance in schizophrenia. Biol Psychiatry 21:249–262

Günther W, Moser E, Müller-Spahn F, v Oefele K, Buell U, Hippius H (1986c) Pathological cerebral blood flow during motor function in schizophrenic and endogenous depressed patients. Biol Psychiatry 21:889–899

Günther W, Breitling D, Moser E, Davous P, Petsch R (1987) Brain mapping, rCBF and MRI measurements of motor dysfunction in tpye I and II schizophrenic patients. In: Takahashi R, Flor-Henry P, Gruzelier J, Niwa S (eds) Cerebral dynamics, laterality and psychopathology. Elsevier, Amsterdam, pp 519:533

Günther W, Davous P, Godet JL, Guillibert E, Breitling D, Rondot P (1988a) Bilateral brain dysfunction during motor activation in type II schizophrenia measured by EEG mapping. Biol Psychiatry 21:295–311

Günther W, Steinberg R, Breitling D, Davous P, Godet JL, Moser E, Petsch R, Heller H, Raith L, Streck P (1988b) Probleme der Lateralität und neurophysiologische Befunde bei Schizophrenien. In: Kaschka WP, Joraschky P, Lungershausen E (eds) Die Schizophrenien. Springer, Berlin Heidelberg NewYork, pp 49–62

Günther W, Moser E, Petsch R, Brodie JD, Steinberg R, Streck P, Raith L (1988c) EEG-mapping, rCBF, NMR and PET in the studies of motor dysfunction in schizophrenia. Abstracts of the XVI CINP Congress, Munich

Hamster W (1980) Die motorische Leistungsserie (MLS); Handanweisung. Schuhfried, Mödling

Karson CN, Kleinman JE, Freed WJ (1982) Blink rates in schizophrenia. In: Usdin E, Hanin I (eds) Biological markers in psychiatry and neurology. Pergamon Press, New York, pp 339–345

Manschreck TC (1986) Motor abnormalities in schizophrenia. In: Nasrallah HA, Weinberger DR (eds) Handbock of schizophrenia. Elsevier, Amsterdam, pp 65–96

Mather JA, Putchat C (1984) Motor control of schizophrenics-II. Manual control and tracking: sensory and motor deficits. J Psychiatr Res 18:287–298

Maurer K, Dierks T (1987) Brain Mapping-topographische Darstellung des EEG und der evozierten Potentiale in Psychiatrie und Neurologie. Z EEG-EMG 18:4–12

Morihisa JM, McAnulty GB (1985) Structure and function: BEAM and computed tomography in schizophrenia. Biol Psychiatry 20:3–19

Norusis MJ (1985) SPSS-X advanced statistics guide. McGraw-Hill Book Company, NewYork

O'Brien RG, Kaiser MK (1985) MANOVA method for analyzing repeated measures designs: an extensive primer. Psychol Bull 97:316–333

Oepen G, Botsch H (1988) SPECT bei Schizophrenie. In: Oepen G (ed) Psychiatrie des rechten und linken Gehirns. Deutscher Ärzte-Verlag, Cologne, pp 147–155

Oldfield RC (1971) The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9:97–113

Overall and Gorham (1976) Brief Psychiatric Rating Scale. In: Guy W (ed) ECDEU Assessment Manual for Psychopharmacology. Rockville, Bethesda, Md. pp 157–169

Petsche H, Rappelsberger P, Pockberger H (1988) Sex differences in the ongoing EEG: probability mapping at rest and during cognitive tasks. In: Pfurtscheller G, Lopes da Silva FH (eds) Functional brain mapping. Huber, Toronto, pp 161–169

Schoppe KJ (1974) Das M-L-S Gerät. Ein neuer Testapparat zur Messung feinmotorischer Leistung. Diagnostica 20: 43–46

Schultz JH (1960) Das autogene Training. Thieme, Stuttgart

Springer SP, Deutsch G (1984) Left brain, right brain. Freeman, New York

Springer SP, Deutsch G (1987) Linkes rechtes Gehirn. Funktionelle Asymmetrien. Spektrum der Wissenschaft, Heidelberg

Sturm W, Büssing A (1985) Ergänzende Normierungsdaten und Retest-Reliabilitätskoeffizienten zur Motorischen Leistungsserie (MLS) Schoppe. Diagnostica 31:234–245

Received October 12, 1988