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Functional EEG mapping and SPECT in detoxified male alcoholics

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Abstract Fifteen alcoholics diagnosed according to DSM-III-R, who were detoxified for at least 2 weeks and showed no clinical withdrawal signs, were investigated with 16 channel EEG mapping during resting, manumotor and music perception conditions, and were compared with 13 control persons. Single photon emission computed tomography (SPECT) using hexa-methyl-propilene-amine-oxime (HMPAO) labeled with 99m-technetium (^{99m}Tc) as tracer was performed separately (in patients only) and submitted to semiquantitative region of interest (ROI) analysis in 2 slices, 6 and 10 cm above canthomeatal line, respectively. Resting EEG showed increased power values in fast beta frequency band for the detoxified alcoholics. On cortical stimulation, patients showed signs of pathological EEG reactivity. Correlations of EEG parameters to cerebral blood flow (CBF) values (patients only) yielded coefficients around zero for all frequency bands (signs of uncoupling). All findings point to organic brain dysfunctions in these patients which extend beyond the period of withdrawal.

Key words EEG mapping · HMPAO-SPECT · Detoxified alcoholics · Brain dysfunction · Functional neuroimaging

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Introduction

Functional neuroimaging in psychiatric disorders may reveal insights into topographic-temporal representations of disturbed mental functions, and indicate patterns of neuronal rehabilitation in various conditions (Brandt 1995), linked to brain plasticity (Brodie 1996). For the clinical psychiatrist, information on disease-specific signs of brain dysfunction, assessed with sufficient sensitivity, may have direct therapeutic consequences, e.g. planning duration of treatment and time course of rehabilitation (Günther et al. 1996a, b). Methods such as single photon emission computed tomography (SPECT) and positron emission tomography (PET) provide, for the time being, an optimal methodology for cross-sectional brain function assessment in psychiatric patients (review e.g. Goldberg et al. 1995). However, due to radiation exposure and/or cost/availability issues, these methods are less suitable for repetitive investigations, which, however, appear to be mandatory for long-term monitoring of brain function. Functional magnetic resonance imaging (MRI) may develop in the future as another possibility for high-quality assessment of certain aspects of brain dysfunction in psychiatric conditions (Schröder et al. 1995; Mager et al. 1996). Thus, for the time being, electrophysiology provides with new EEG and evoked-related potential (ERP) technologies and computer-based evaluation a source of information with its own merits: these methods are of low cost, easily accessible and, above all, completely innocuous in studies of long-term disease course in humans.

In a first series of investigations we used a 16-channel EEG system (Cartovar I, Alvar, Paris, France) and SPECT as external validation. The last investigation of this series is reported in this paper, whereas the (ongoing) 32-channel EEG cross-validation studies are reported separately for space reasons. Whereas visual EEG evaluation in alcoholic patients yields only inconclusive findings (e.g. Kugler 1981; Peter et al. 1994), more information is available using quantitative EEG.

Relative and absolute amounts of slow and fast frequencies seem to be elevated in some chronic alcoholics, whereas alpha seems to be diminished (Little and McAvoy 1952). Increased delta and theta power may reflect permanent changes in brain function due to prolonged excessive alcohol use (Johannesson et al. 1982; Spehr and Stemmler 1985), whereas deficient alpha (Propping 1983) and decreased beta (Gabrielli et al. 1982) may be associated with a biological predisposition to develop alcoholism.

Other differences in comparison with normal persons, such as increased beta, may indicate withdrawal of short (days to weeks) duration (Coger et al. 1978), whereas even after 5 years of abstinence abnormal findings in theta may persist (Pollock et al. 1992).

Longitudinal studies using quantitative EEG may be useful in order to disentangle these alternative interpretations. Including resting and activation conditions increases sensitivity and specificity to detect chronic alcoholics vs normal and various psychiatric groups (Günther et al. 1996a), as is also indicated by abnormal findings during visually and acoustically ERP findings (Hegerl et al. 1995; Kathmann et al. 1996).

Acute alcohol administration raises cerebral blood flow (CBF) in most brain regions, predominantly in right frontal areas, in normals (Tiihonen et al. 1994) and alcoholics (Mathew and Wilson 1991). Chronic consumption, in contrast, appears to be associated with reduced CBF, especially in grey matter (Rogers et al. 1983), which may improve after weeks to months of abstinence, as shown by SPECT (Hata et al. 1987; Meyer et al. 1985) and PET methods (Volkow et al. 1992). However, as in the quantitative EEG studies outlined above, much remains to be elucidated to separate circulatory and metabolic effects of pre-existing biological abnormalities, those of long-lasting intaken and withdrawal (Caspari et al. 1993) as well as their time course (Sclafani et al. 1995).

Thus, the hypotheses of our combined EEG/SPECT investigation in detoxified chronic alcoholics can be stated as follows:

1. Applying our resting-motor/music perception paradigm yields EEG changes which are not found in normal persons nor other clinical control groups (schizophrenic and Gilles de la Tourette patients).
2. Even in the absence of any gross abnormalities of CBF there may be signs of deviant correlations between EEG and CBF.
3. Both quantitative functional EEG findings alone, as well as signs of rCBF/EEF "uncoupling", may indicate subtle brain dysfunction in these patients extending well beyond the period of withdrawal.

Materials and methods

Subjects

Fifteen consecutively admitted chronic alcoholics were recruited from the detoxification unit at the Psychiatric University Hospital in Munich (Germany). All patients fulfilled the diagnostic criteria for alcohol dependence both according to ICD-9 (303.9) and DSM-III-R (303.90), with a duration of the dependence of at least 10 years. Patients were only admitted to the study after a minimum of 14 days detoxification and if clinical examination revealed neither vegetative (sweating, trembling) nor psychopathological (hallucinations, paranoid ideation) symptoms of withdrawal. Furthermore, no drug treatment was allowed for at least 1 week prior to investigation, except substitution of B 1/6 vitamins. Further inclusion/exclusion criteria were: 18–60 years of age (average age 44.8 years, range 34–56 years), no history of head trauma or organic brain disease including seizures, no pathological findings on clinical evaluation of MRI/CT and SPECT (if performed). No female subjects were admitted to the study, since we definitively wished to avoid exposure of pregnant women to radiation hazards (SPECT). Due to our functional challenges involving manumotor and music perception tasks, all subjects were required to have normal hearing abilities and patients with neurological and/or surgical-orthopaedic reasons for diminished psychomotor performance (including severe polyneuropathy involving the upper limb) were not eligible. All subjects had to be right handed (9–10 positive answers on the shortened version of the Edinburgh scale (Oldfield 1971). Control persons were 13 male medical students and members of the hospital staff (mean age 44.1 years, range 20–57 years) chosen according to the above inclusion/extension criteria, who were carefully screened for the absence of substance misuse and instructed to remain without alcohol and/or other psychotropic substances for at least 24 h prior to investigation. There was no statistical difference in age (see above) or years of education in alcoholics vs control persons (12.4 years, SD 2.5 years, vs 13.1 years, SD 2.2 years, respectively) on *t*-test screening.

EEG methods

A 16-channel EEG cartography system (Alvar Cartovar I, average reference, time constant 0.3-s, band pass filter 0.5–30 and selective filter 50 cps, digitalization rate 128 cps, artefact exclusion off-line, FFT calculations in artifact "free" – as far as possible – 6-s segments in steps of 0.5 cps from 0.5 to 30 cps) was used for EEG mapping investigations, which has been described in full detail (Günther et al. 1993a).

After obtaining informed consent, every patient was studied either on the day of inclusion or the day after. Whenever possible, approximatley the same time range in the morning was applied for the investigation of all alcoholic and normal subjects. The persons were seated in a light- and sound-protected room in an EEG investigation chair. Subjects could be observed during the whole investigation by the technician. Music tasks were provided binaurally by earphones. Eyes were closed during all resting state and activation situations. Subjects were carefully instructed to avoid, as far as possible, movements of eyes and lid, as well as voluntary tension of muscles.

Investigation procedure

After 5 min routine EEG recording (both to obtain a clinical EEG and to adjust the patient to the EEG investigation situation), the following sequences were registered:

1. Calibration (10 × 6) s
2. Resting condition 1 (10 × 6) s
3. Hand right (repetitive fist opening with the dominant right hand (frequency 1/s) (10 × 6) s
4. Resting 2 (10 × 6) s
5. Hand left (10 × 6) s
6. Resting 3 (10 × 6) s
7. Music 1 (rumba rhythm) (10 × 6) s
8. Resting 4 (10 × 6) s
9. Music 2 (rumba rhythm as an arpeggio with cadence) (10 × 6) s
10. Resting 5 (10 × 6) s

The total duration was 10 min.

SPECT measurements

SPECT imaging was done 90 min after intravenous injection of 550–750 milli-Bequerel (mBq) ^{99m}Tc-HMPAO. The dosis used in a particular person was adjusted to body weight to approximate 10 mBq per kg. 99m-technetium-HMPAO is a lipophilic substance which readily crosses the blood-brain barrier and is deposited according to CBF into brain tissue. Imaging was performed using a rotating gamma camera (single head; General Electric Maxi II) yielding 12 axial slices, thickness 1 cm, starting from the canthomeatal line. Subjects were investigated in a sound- and light-(dimmed) protected room. Image acquisition time was 30 min, yielding an overall investigation time of 60 min together with a 30-min waiting period after bolus injection. Special moulded headholders were adapted in order to place the subjects, head reproducibly. As pointed out previously (exclusion criteria), clinical evaluation by one of us (P.K.) yielded no pathological asymmetries or other abnormalities of flow in either level which would have excluded the subjects from further study. (Only one clinical subject had to be excluded for such reasons.)

Slices 5 and 9 (6 and 10 cm above cantomeatal line, respectively) were used for semiquantitative region of interest (ROI) analysis. Size of ROI was 3.75 × 3.75 cm (equalling 6 × 6 pixels). Maximal, minimal and total count, as well as total number of pixels and average flow (total count divided by total number of pixels), were calculated by computer algorithm. Average flow was used for further statistical analysis in the following manner. Following an own methodology establishing correlations between EEG and glucose uptake measured by PET (Günther et al. 1993c) and in accordance with similar methodology establishing correlation coefficients between EEG and SPECT (Frölich et al. 1993; Kwa et al. 1993), we established ROIs in the previously defined image level 2 (subcortical) in a fixed strategy: the outer corners of regions FP1, FP2, Oz, T3 and T4 coincided with the outer rim of the SPECT image. Regions F7, F8 and T5, T6 were positioned exactly in the middle of the above ROIs as assessed by two independent experts. Similarly, in the cortical level all six ROIs matched the outer rim of the SPECT image and were positioned symmetrically and equidistantly (Fz and Pz being fixed first).

The procedure of independently establishing ROIs was established in a preceding 6 patients yielding a correlation coefficient of

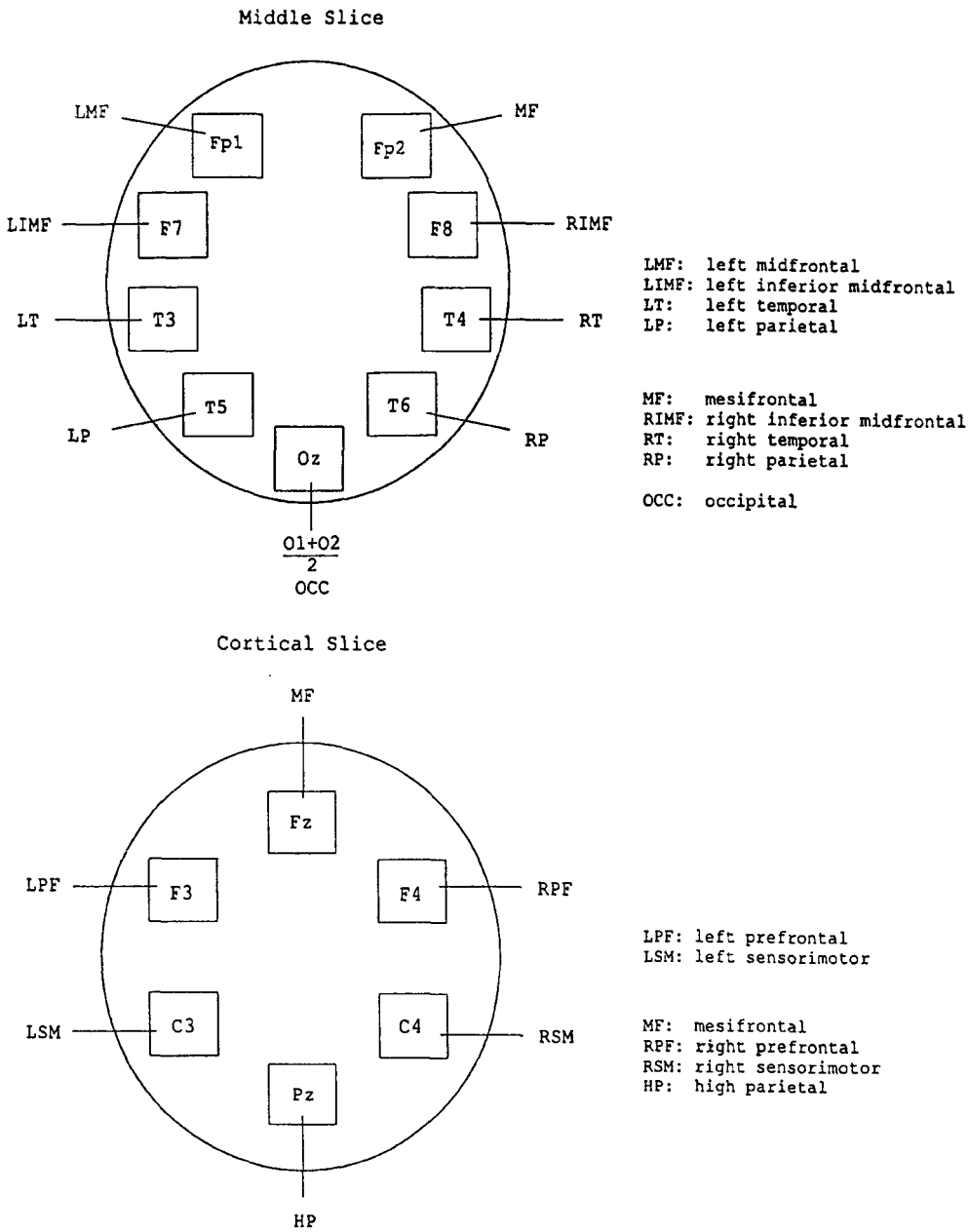

Fig. 1 Regions of interest: middle and cortical slice

0.93 for the two experts measures with regard to the average ROI flow. A schematic display of these fixed ROIs which were related to reproducible electrode positions as defined by the 10/20 system is demonstrated in Fig. 1.

Average flow values were normalized to EEG values in the following manner: the percentage of average flow to the total flow was calculated for each ROI, using an analogous procedure as for the relative proportion of power to the total power in the frequency bands of computerized EEG, respectively. Subsequently, Pearson's product moment correlations were calculated between these normalized percentage SPECT and EEG values (full details of the methodology in Stieg 1996).

As pointed out previously, a semiquantitative SPECT evaluation in comparison with a normal control group was *not* possible due to ethical problems in administering radioactive substances to healthy persons and was beyond the scope of our investigation.

Results

EEG mapping

EEG evaluation/resting conditions and statistical analysis

Of the ten 6-s segments of each condition, a minimum of two was required which was considered artefact free in order to provide the basis for average power histograms. This minimum of two 6-s segments was available in all patients but one (who had to be excluded from the study) and all normal control persons. For data reduction the values were treated in the following (conventional) frequency bands: delta 0–4.5, theta 5–7.5, alpha 8–13.5, beta 1 14–20.5, beta 2 21–30. The average values over all electrodes (grand means) for each frequency band in eyes closed/resting conditions are displayed in Table 1.

As can be seen from Table 1, patients showed higher power values in all frequency bands with high variances in both groups. For a statistical screening, Kolmogorov-Smirnov tests were used in a first step in order to control for normal distribution of the data (Clauss and Ebner 1985). We found Z-values between 0.609 and 1.181; none of them reached significance ($p = 0.01$), thus indicating normal distribution of data. This precondition established, we subsequently performed five t-tests for independent samples using an algorithm for unequal variances (Clauss and Ebner 1985, p 212). The t-values for alpha ($t = 2.23$, $p < 0.05$), beta 1 ($t = 2.81$, $p < 0.05$) and beta 2 ($t = 3.55$, $p < 0.01$) were significant. However, after correcting for multiple testing using the Bonferroni formula, only the differences for the beta-2 band remained significant. Consequently, only this difference (which is in line with several reports in the literature) are considered as established in a preliminary fashion and cross-validation results seem to be required in order to further corroborate our EEG findings, which are ongoing.

Table 1 Resting conditions results. Average power values and standard deviation in five conventional frequency bands for alcoholic (Alc) and control (Cnt) persons

		Alc ($n = 15$)	Cnt ($n = 13$)	p[a]
Delta	x	95.93	140.25	n.s.
	s	(51.51)	(83.22)	
Theta	x	30.13	20.56	n.s.
	s	(26.37)	(4.24)	
Alpha	x	164.08	95.25	n.s.
	s	(110.91)	(42.00)	
Beta 1	x	62.06	32.25	n.s.
	s	(40.58)	(6.31)	
Beta 2	x	43.87	31.63	< 0.05
	s	(8.56)	(9.56)	

[a] After controlling for normal distributions (Kolmogorov-Smirnov tests), t-tests for unequal variances were performed and probabilities corrected for multiple testing using Bonferronis formula

EEG evaluation/activation conditions and statistical analysis

Multifactorial analyses of variance were calculated for repeated measurements for each frequency band ($n = 5$), for the factor tasks ($n = 8$; not included were the calibration period and the last resting period) and 16 electrodes separately for each group (direct comparisons were not performed, since in several frequency bands there were major differences for resting conditions already, as indicated previously, which might cover subtle differences during cortical activation). The calculations included first-rank interactions (task × electrode) only, using the SPSS/PC statistical evaluation program. This multivariate statistical procedure provided the basis for the subsequent t-test analysis and probability mapping. (Details of this statistical procedure are discussed in Günther et al. 1989, 1993 a).

The values for the MANOVAS are given in Table 2.

As can be seen from Table 2, the factors "task" and "electrode" became significant in nearly all frequency bands for both groups indicating that task effects were present in all frequency bands and were not the same in all electrodes, which is analysed below.

Table 2 Multivariate analysis of variance (repeated measures) contrasting (between) alcoholic (Alc) and control (Cnt) subjects within factors "task" ($n = 8$) and "electrode" ($n = 16$) in five frequency bands

	p-value				
	Delta	Theta	Alpha	Beta 1	Beta 2
Alc ($n = 15$)					
Task	0.000	0.000	0.000	0.843	0.012
Electrode	0.000	0.000	0.000	0.000	0.000
Cnt ($n = 13$)					
Task	0.000	0.000	0.000	0.000	0.000
Electrode	0.000	0.000	0.000	0.000	0.000

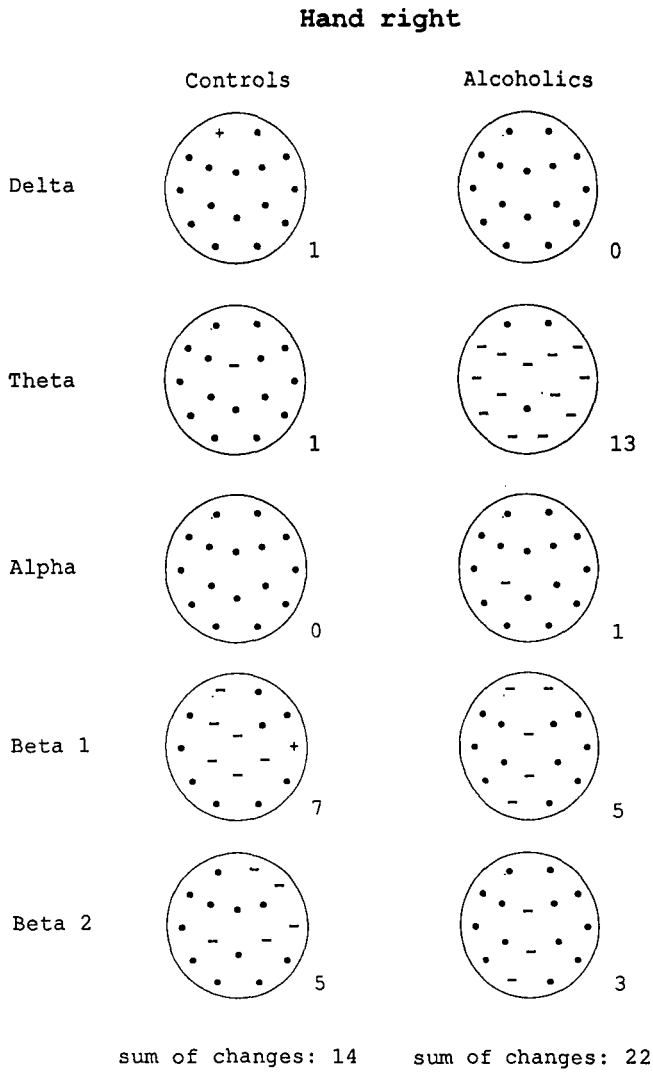

Fig. 2 Changes in manumotor right activity at *t*-test screening in healthy controls and alcoholics. For electrode placement see Table 3 (10/20 system: schematic display not to scale). + significant increase; – decrease; • no change

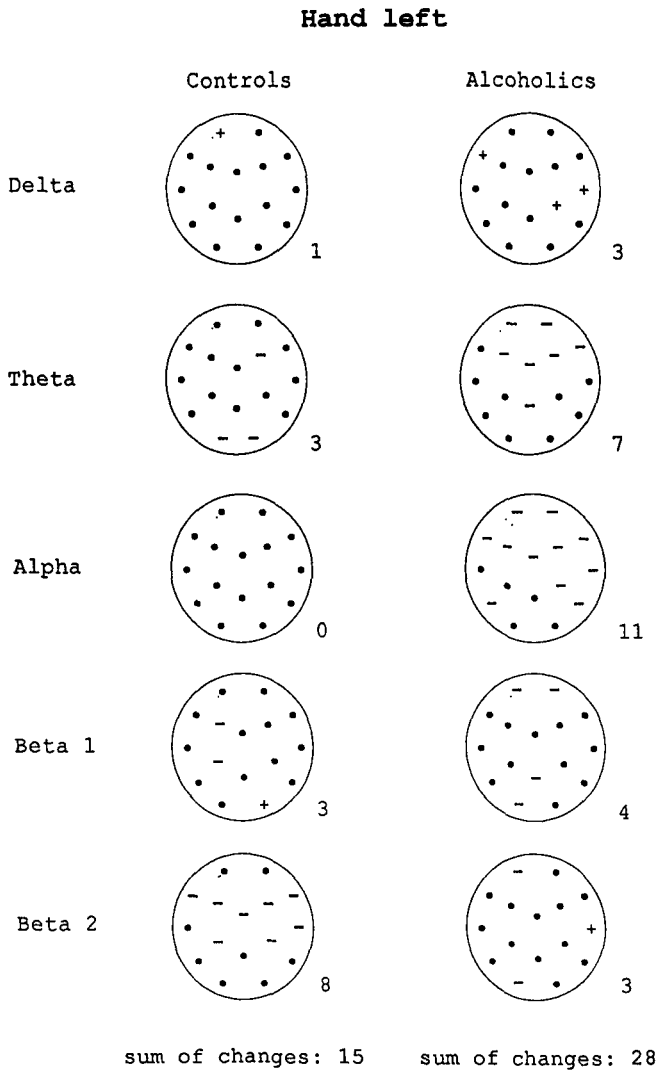

Fig. 3 Changes in manumotor left activity at *t*-test screening in healthy controls and alcoholics. For electrode placement see Table 3 (10/20 system: schematic display, not to scale). + significant increase; – decrease; • no change

Psychomotor activation

Due to sequential brain activation the resting conditions showed notable changes during the whole activation procedure (cf. Klages 1991, p. 29). Therefore, we compared every activation procedure to the immediately preceding reference resting condition.

Figures 2 and 3 display the power changes in hand right and hand left motor activation conditions. As can be seen from Figs. 2 and 3, alcoholics show EEG changes which are different to healthy control persons and thus considered pathological. Maximal differences are observed in theta frequency band for "hand right" and in alpha frequency band for "hand left" (alcoholics show more reductions). Only minor differences in EEG changes are found in the other bands.

Music perception activation

Figures 4 and 5 display EEG changes on simple and complex music perception. As can be seen from Fig. 4 and 5, alcoholics display in these activation conditions pathological EEG changes also. For both music perception tasks, these involve mainly the alpha frequency band, in which normal persons increase their power values (more relaxation?), whereas alcoholics do not.

Both abnormal EEG changes (to manumotor and music perception) conditions seem to indicate pathological brain function in detoxified alcoholics suggesting speculatively a sort of overactivation/overarousal, extending well beyond the period of detoxification. The findings appear to be diffuse, not affecting certain areas of the brain in predominance.

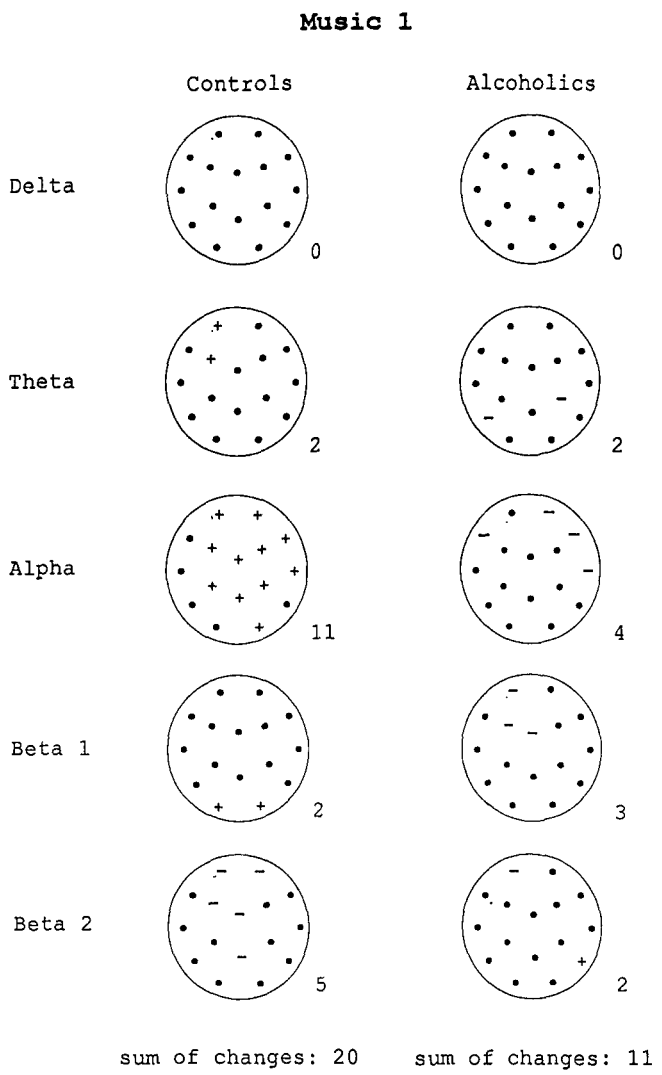

Fig. 4 Changes in simple music perception at *t*-test screening in healthy controls and alcoholics. For electrode placement see Table 3 (10/20 system: schematic display, not to scale). + significant increase; – decrease; • no change

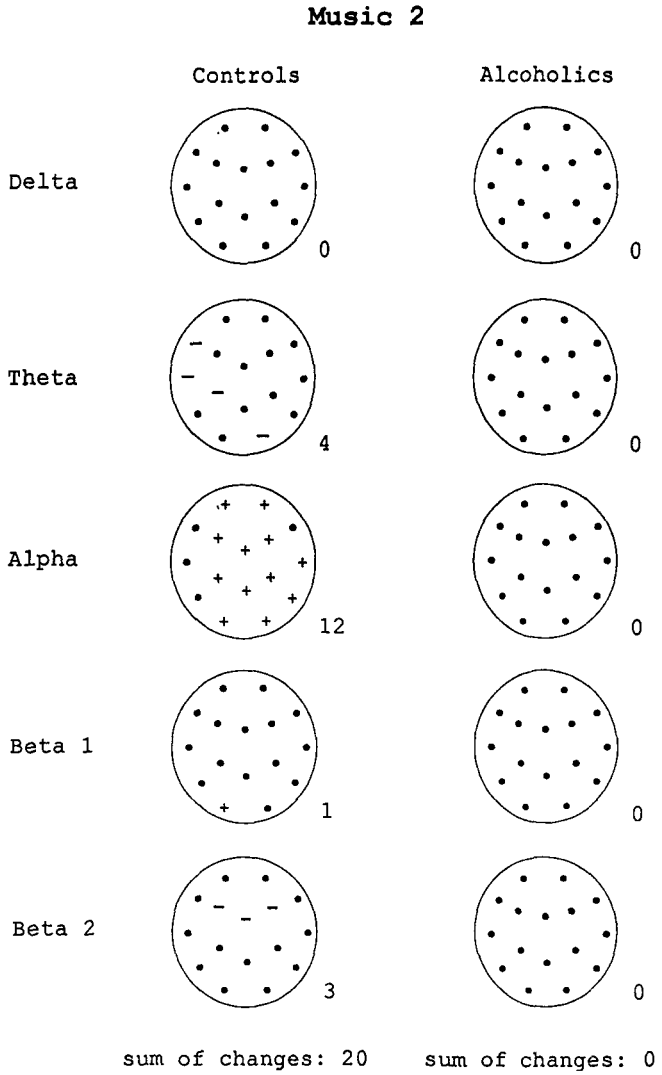

Fig. 5 Changes in complex music perception at *t*-test screening in healthy controls and alcoholics. For electrode placement see Table 3 (10/20 system: schematic display, not to scale). + significant increase; – decrease; • no change

Correlations of EEG mapping (resting conditions)/SPECT

Due to the ethical reasons which have been stated previously, no normal control group was investigated using SPECT. Additionally, since only correlations between values of the EEG and SPECT in the semiquantitative ROIs of the two slices under study were assessed, comparisons with normal SPECT measurements were impossible and beyond the scope of this investigation.

Table 3 displays the correlation coefficients between EEG power and semiquantitative flow measurements in detoxified alcoholics. As can be seen from Table 3, there are correlation coefficients around zero only (from –0.3082 to +0.3223). This is not to be expected from findings in the literature (for a recent editorial on this issue see Dager and Swann 1996), indicating that EEG (power) and blood flow are tightly coupled in normals (although with a time delay, which should not matter in our functional steady-state study; Brandt 1995). This finding is consequently considered as a further sign of organic brain dysfunction (uncoupling) in detoxified alcoholics.

Discussion

Quantitative EEG investigations in 15 chronic alcoholics revealed both in resting and functional activation conditions, as well as by complete lack of coupling to CBF as assessed by ^{99m}Tc-HMPAO SPECT, signs which are speculatively indicative of organic brain dysfunction (as compared with normals), lasting well beyond the phase of acute detoxification. However, before discussing these results further, several methodological limitations have to be addressed.

Table 3 Correlation coefficients between EEG power and regional average flow in the respective region of interest. MF mesifrontal; RPF right prefrontal; RSM right sensorimotor; LMF left midfrontal; LPF left prefrontal; LSM left sensorimotor; OCC occipital; RIMF right inferior midfrontal; RT right temporal; RP right parietal; MF mesifrontal; LIMF left inferior midfrontal; LT left temporal; LP left parietal; HP high parietal

Region of interest	Electrode position	Delta 0.5–4.5	Theta 5.0–7.5	Alpha 8.0–13.5	Beta 1 14.0–20.5	Beta 2 21.0–30
MF	Fp2	–0.3083	–0.1278	0.0656	0.0857	0.0289
RPF	F4	–0.2366	–0.2263	0.1293	0.1244	0.2173
RSM	C4	–0.0549	–0.0514	0.1677	0.1938	0.1780
LMF	Fp1	–0.1488	–0.1628	0.0953	0.0555	0.0279
LPF	F3	–0.0505	–0.1764	0.0209	–0.0249	0.0225
LSM	C3	–0.2008	–0.1755	0.0053	0.0765	0.0443
OCC	Oz	0.0855	–0.0431	0.2549	0.2758	0.3121
RIMF	F8	–0.1192	–0.1825	0.1263	0.2316	0.1814
RT	T4	–0.0866	0.0739	0.1842	0.1549	0.1855
RP	T6	–0.0063	–0.0164	0.0078	0.1397	0.1763
MF	Fz	–0.1854	–0.1749	0.0097	–0.0361	0.1859
LIMF	F7	–0.0173	–0.1465	0.0981	0.1068	0.1214
LT	T3	–0.2112	–0.1400	0.1415	0.2125	0.2815
LP	T5	–0.1511	–0.0760	0.1789	0.3006	0.3223
HP	Pz	–0.1432	–0.1743	0.0892	0.0913	0.1428

Methodological problems inherent to any EEG investigation, such as eye and muscle artefact contamination, cannot be resolved perfectly (only as far as possible), as has been discussed in detail, for example, in Günther et al. 1993 a (p. 524).

Furthermore, as pointed out also by John et al. (1988, 1994), the topographical resolution of EEG mapping remains limited, as well as the knowlege of the contribution of deeper cortical dipoles to a given electrical field measured on the skull (Herrmann and Winterer 1996).

This advises caution in the interpretation of single findings, especially when relations between two imaging methods are assessed. These results may be further obscured by non-reproducible positioning of the head, different states of psychopathology and arousal and more possible sources of bias. However, despite the fact that most of these problems are again not avoidable on a 100% level, the reliability and validity of findings may be supported by other scientific evidence. Firstly, it adds evidence if several unrelated findings within the same investigation point towards similar conclusions. Secondly, and more importantly, consistent results of other studies and methods, applied by other research groups, may support our findings both directly and indirectly.

Both lines of support can be obtained from the literature. Both resting EEG and changes during cortical activation are distinctly different in detoxified alcoholics and normal controls. As the resting values are concerned (fast beta increases), we are unable to decide at this time whether they are due to: (a) long-lasting though discontinued alcohol intake as proposed by Johannesson et al. 1982, and Spehr and Stemmler 1985; (b) still ongoing influences of discontinuation/withdrawal (which may last longer than 5 years; Pollock et al. 1992); (c) a biological predisposition to alcohol misuse (Propping 1983); (d) and/or a combination of these or possible other sources of variance. However, both resting and activation EEG findings remain different from those obtained in normals, and in other psychiatric patients, which supports our first hypothesis stated above.

If one is ready to assume that EEG is linked (in complex ways) to electrical aspects of neuronal function of the brain, then this points to brain dysfunction in detoxified alcoholics, which remains longer demonstrable by EEG than by clinical (vegetative and/or psychopathological) assessment. Such brain dysfunction can be demonstrated with extremely high sensitivity and seems, encouragingly, to be highly specific also (Günther et al. 1996 a). The discriminant variables separating various patient groups can only be outlined here for space reasons. Resting conditions alone cannot produce acceptable high sensitivity or specificity (Günther et al. 1996 a). This may – among other sources – be due to minor stability of resting/eyes closed and related EEG analysis conditions in groups of patients, whereas such conditions seem to be better reproducible in normal persons (John et al. 1988, 1994). However, during cortical activation we observed EEG changes which were greatly different in various patient groups and better reproducible than resting conditions (less variability in activation?; Günther et al. 1989). The distinct, diffuse reductions of alpha power in simple manumotor tasks (Figs. 2, 3) which were exhibited by the detoxified alcoholics correspond well to a reduced response to the relaxation effects induced by music perception (Figs. 4, 5). This is interpreted speculatively as overarousal in these patients. Such a pattern is not seen, for example in schizophrenics (who show on the same stimulation a nearly complete nonreactivity, especially in negative patients; Günther et al. 1993 a), which seems similar to that shown by demented patients of the Alzheimer type (Günther et al. 1993 b). Still other changes/differences are found in Gilles de la Tourette patients (functional non-reactivity combined with normal resting power values; Günther et al. 1996 b).

Although more evidence with these resting/activation EEG studies is needed, our paradigm appears to provide sufficient sensitivity and specificity in assessing diffuse brain dysfunctions for deserving further evaluation in longitudinal brain function monitoring studies.

The lack of correlations between EEG and blood flow/SPECT parameters found in this investigation (in line with our second hypothesis) is also interpreted – speculatively – as indicating diffuse brain dysfunction in detoxified alcoholics. Although methodological shortcomings, as outlined previously, may have diminished correlations between EEG power and SPECT, this appears insufficient to explain the complete lack of correlations alone, viewing the following considerations:

Firstly, we followed a similar strategy linking EEG and 99mTc-HMPAO SPECT as Frölich et al. (1993; reference: linked ears) and Kwa et al. (1993; bipolar leads) in demented patients, and Molina et al. (1995) in obsessive-compulsive patients. Despite the fact that positioning problems and other biases (different references) should have been similar to ours in these investigations, blurring possibly higher correlations between both parameter sets, both groups found around zero correlations only in some topographical regions and highly positive and negative ones in others. This supports the assumption that our zero correlations in virtually all brain regions under study, despite controlling for absolute power (by using only the percentage of power distribution), may not be explained by methodological shortcomings alone, but supports a potential validity of our findings.

Secondly, a tight coupling of EEG and rCBF as assessed by SPECT (and or PET) is well established when sufficient care is taken to have comparable "time windows" (Brandt 1995; Dager and Swann 1996). This should also be the case in our study, where steady-state conditions (1 min resting EEG) were compared with the summarized cerebral uptake of the labeled HMPAO, although – definitely – the time frame remains different (1 min vs minutes of steady-state building up the summed CBF values). However, with a similar design linking power values obtained in 10/20 EEG locations and fixed ROI evaluation of 11-CDG uptake measured by PET, the correlation coefficients used the full range from nearly –1 to nearly +1 in schizophrenics (Günther et al. 1993c) and normal controls (Alper et al. 1994, and in preparation).

Finally, further support to the validity of diffuse pathological coupling between EEG and rCBF may also be obtained by findings obtained with SPECT and PET alone.

In several SPECT/PET studies, acute intake of alcohol as well as acute withdrawal (up to 3 weeks) revealed circumscribed increases in blood flow in frontal and temporal regions, speculatively linked to activation of dopamine-dependent reward systems (Tiihonen et al. 1994; Caspari et al. 1993). However, chronic administration seemed to reduce blood flow (Rogers et al. 1993; Wang et al. 1992) and glucose consumption diffusely (Volkow et al. 1992), though with a predominance in subcortical, left parietal and bifrontal regions. After long-lasting withdrawal, these hypometabolic areas increased their metabolism in all regions except in the basal ganglia (Volkow et al. 1994).

Evidently, this connects long-lasting PET/SPECT signs of alcohol misuse to those of brain atrophy and cognitive dysfunction found even years after cessation of alcohol consumption (Sclafani et al. 1995). Prospective follow-up studies seem urgently needed in order to obtain better information on the time course and reversibility of such alcohol-related signs of brain dysfunction in subgroups of alcohol patients. Functional EEG mapping may be a promising candidate method for this purpose and deserves further evaluation.

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