Beta Power in the EEG of Alcoholics

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Background: *In this study, the magnitude and spatial distribution of beta power in the resting electroencephalogram (EEG) were examined to address the possibility of an excitation–inhibition imbalance in the central nervous system of alcoholics.*

Methods: *Log transformed absolute power in the Beta 1 (12.5–16 Hz), Beta 2 (16.5–20 Hz), and Beta 3 (20.5–28 Hz) bands in the eyes-closed EEG of 307 alcohol-dependent subjects and 307 unaffected age- and gender-matched control subjects were compared using a multivariate repeated measures design. Effect of gender, age, and drinking variables was examined separately.*

Results: *Increased Beta 1 (12.5–16 Hz) and Beta 2 (16.5–20 Hz) absolute power was observed in alcohol-dependent subjects at all loci over the scalp. The increase was most prominent in the central region. Increased Beta 3 (20.5–28 Hz) power was frontal in the alcoholics. Age and clinical variables did not influence the increase. Male alcoholics had significantly higher beta power in all three bands. In female alcoholics the increase did not reach statistical significance.*

Conclusions: *Beta power in all three bands of resting EEG is elevated in alcoholics. This feature is more prominent in male alcoholics. The increased beta power in the resting EEG may be an electrophysiological index of the imbalance in the excitation–inhibition homeostasis in the cortex.* Biol Psychiatry 2002;51:831–842 © *2002 Society of Biological Psychiatry*

Key Words: Beta, electroencephalogram, alcoholism, absolute power, gender, inhibition

Introduction

EEG and Beta Rhythm

Beta oscillation in the electroencephalogram (EEG) has been extensively studied in resting states of normal and pathologic conditions of the central nervous system (Neidermeyer 1999). Rhythmical activity from 13 Hz to 30 Hz, designated as the *beta frequency band*, is considered as an index of cortical arousal. Beta frequencies can be functionally categorized into active and resting beta, depending on the context in which the EEG is recorded. Physiologically these frequencies are categorized on the basis of their topography into four types: 1) frontal beta, which is most commonly reported and consists of fast frequencies; 2) central beta, which is partly the basis of rolandic mu rhythm and is found mixed with mu rhythm; 3) posterior beta, which is often a fast alpha equivalent; and 4) diffuse beta, which is not linked to any special physiologic rhythm (Neidermeyer 1999). In human EEG, frequencies in the beta range are synchronized during multimodal integration over larger areas of the scalp (von Stein et al 1999). Active beta rhythms, along with faster gamma rhythms (>30 Hz), have been recorded in association with attention, perception, and cognition (Haenschel et al 2000; Singer 1993; Wróbel 2000).

Many drugs produce either an increase of beta activity in the resting EEG, most conspicuous over frontal regions, or alter the frequency of the dominant rhythm, more clearly seen posteriorly. In particular, the benzodiazepines and barbiturates produce strong increases in beta power (Domino et al 1989; Feshchenko et al 1997). The primary sites of action in the central nervous system (CNS) of these drug classes are the receptors of the inhibitory neurotransmitter γ-aminobutyric acid, type A ($GABA_A$) (Tobler et al 2001). Extensive experimental and modeling studies have contributed in defining neuronal substrates of fast—gamma (>30 Hz) and beta (12–30 Hz)—oscillations (Kopell et al 2000; Whittington et al 2000b). These studies suggest that fast oscillations are produced by complex interactions within small networks involving the excitatory pyramidal cells and the inhibitory interneurons. These interactions between excitatory pyramidal cells and

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inhibitory interneurons could be the possible sites of action for the modulatory influences of certain psychoactive drugs (Whittington et al 2000a).

EEG and Alcoholism

Etiologic factors associated with the predisposition to develop alcohol dependence remain a focus of substantial research efforts. Quantified of fundamental neurobiological/neurobehavioral characteristics associated with alcoholism, such as EEG, can serve as endophenotypes (Begleiter and Porjesz 1999), which can be used in conjunction with diagnostic criteria to substantially improve phenotypic definition.

Studies that have attempted to define the EEG characteristics of alcoholics (Begleiter and Platz 1972; Propping et al 1981) have been fairly consistent in their results: most studies report increased beta power (Bauer 1994; Costa and Bauer 1997; Propping et al 1981; Winterer 1998). Propping et al (1981) reported differences in female but not male alcoholics, in whom more beta and fewer theta waves, especially in the anterior–central locations, and a nonsignificant lower number of alpha waves were reported. The mean amplitude of alpha, beta, and theta bands was also examined, and no significant differences were noted. Pollock et al (1992) studied older recovered alcoholics (35–75 years) along with age-matched control subjects and found only theta band differences between groups, marked in the anterior regions of the scalp. We have recently reported increased theta power in the resting EEG in the same large sample of 307 alcoholics used in the present beta analyses. The differences we observed in theta power were more marked posteriorly (Rangaswamy et al, unpublished data).

EEG and High-Risk Subjects

Most studies report differences in the alpha and beta frequency range in the resting EEG spectral profile of high-risk subjects. Significantly increased fast activity (18–26 Hz range) was reported in male but not female high-risk compared to low-risk children of alcoholics (Gabrielli et al 1982). A later EEG study by Pollock et al (1995) reported elevated beta power in family history positive (FHP) when compared to family history negative (FHN) nonalcohol dependent relatives, and this finding was more robust in male high-risk subjects. Ehlers and Schuckit (1991) reported more energy in baseline fast alpha in FHP subjects compared with FHN subjects and a greater decrease in energy in the fast alpha band in FHN subjects post-ethanol challenge. The authors also correlated the increase in absolute beta (12–20 Hz) activity in baseline EEG to drinking history (Ehlers and Schuckit 1990; Ehlers et al 1989). Bauer and Hesselbrock (1993) reported enhancement in resting beta power in nonalcoholic FHP men with antisocial personality disorder. A recent study (Finn and Justus 1999) that examined resting EEG in high-risk subjects reported reduced absolute alpha power in frontal and occipital leads and increased relative beta in FHP individuals when compared to age- and gender-matched FHN individuals. Evidence from all these studies suggests that beta power elevation in resting EEG may be a marker of susceptibility to developing alcoholism; however, there are some studies that report no differences in resting EEG between offspring of alcoholics (high risk) and offspring of nonalcoholics (low risk) (Cohen et al 1991; Kaplan et al 1988; Pollock et al 1983).

Current Study

Our study examines differences in the resting EEG spectrum of theta (3–7 Hz), alpha (8–12 Hz), and beta (12–28 Hz) of alcoholics and unaffected control subjects. Each of these major frequency bands of the EEG has specific functional significance and varying distribution characteristics over the scalp (Neidermeyer 1999). We have previously reported the theta band profile in the same subject sample (Rangaswamy et al, unpublished data). In this article, we report the differences observed in the absolute power of the Beta 1 (12.5–16 Hz), Beta 2 (16.5–20 Hz), and Beta 3 (20.5–28 Hz) bands of the resting EEG of alcoholics in comparison to nonalcoholic, age- and gender-matched control subjects. We examined the magnitude of differences in absolute power of the three beta bands both globally and regionally to assess the topographic differences between groups. Group differences in the relationship between absolute beta power and age were also examined. We also examined the effect of drinking variables (recency of last drink and quantity of drinks in a typical week) on the absolute power in the three beta bands to assess if drinking variables per se influenced group differences (i.e., state related). Finally, we also explored the gender differences in the distribution and magnitude of all three beta bands.

Methods and Materials

Subjects

Subjects were participants in the ongoing Collaborative Study on the Genetics of Alcoholism (COGA) study, a multisite national consortium designed to study the genetics of alcoholism. The collaborative sites are located at State University of New York (SUNY)-Health Science Center at Brooklyn; University of Connecticut Health Center; Washington University School of Medicine in St. Louis; University of California at San Diego; University of Iowa; and Indiana University Medical School. All subjects signed informed consent forms before recruitment into the study. The institutional review board at each site approved

Table 1. Sociodemographic and Clinical Characteristics of the Sample

	Alcoholics		Control Subjects	
	Male	Female	Male	Female
Number	150	157	150	157
Mean age (y) (SD)	32.44 (9.68)	32.47 (7.80)	32.48 (9.75)	32.47 (7.84)
Typical weekly drink total: Mean[a]	21.1	10.13	2.38	1.13
Maximum drinks in 24 hours[a]	32.09	18.68	13.67	6.70
% cocaine dependence–DSM-III-R	34	43	1.3	1.9
% marijuana dependence–DSM-III-R	50	29.9	3.3	6.4
% stimulant dependence–DSM-III-R	20.7	10.2	0	.6
% sedative dependence–DSM-III-R	10	8.3	0	0
% lifetime depression–DSM-III-R	14	19.1	10.7	24.2
% ASP-DSM-III-R	24	6.4	3.3	0

ASP, antisocial personality.
[a]One drink is defined as 1 shot glass of hard liquor; 1 glass of wine; 1 bottle of beer (one drink = approximately 9 gm of absolute alcohol).

the research procedures in the COGA study, and written consent was obtained from each individual before participation. Alcoholic probands were recruited from inpatient and outpatient treatment facilities. A detailed description of the COGA recruitment procedure has been described previously (Begleiter et al 1995). Control families were "randomly" ascertained to be representative of the general population at each of the six sites. Subjects were recruited from health maintenance organizations, drivers license records, and dental clinics. Control subjects were not excluded based on psychiatric illness or alcoholism, to obtain prevalence rates similar to the general population. Subjects were excluded from the neurophysiological assessment if they manifested uncorrected sensory deficits, hepatic encephalopathy/cirrhosis of the liver, significant head injury/seizures, if they had acute/chronic illness and were on medication that affects/influences brain functioning, had a positive breath analyzer test, had undergone neurosurgery, tested positive for human immunodeficiency virus, or had used psychoactive substances in the past 5 days.

A subsample of alcoholic and control subjects was selected from the available COGA database. The alcoholic group consisted of 307 individuals from 174 stage II families (age range: 18–50 years), with a positive diagnosis of alcohol dependence (COGA criteria). The control group consisted of 307 unaffected individuals from 159 randomly ascertained control families, who were screened and assessed to be negative for a diagnosis of alcohol dependence (COGA criteria). Control subjects were age matched (up to 1 year difference) and gender matched to the alcoholic subjects (Table 1).

Data Recording

All six collaborative sites used the same experimental procedures and EEG acquisition hardware and software. Subjects were seated comfortably in a dimly lit, sound-attenuated, temperature-regulated booth (Industrial Acoustics Company, Bronx, NY), and instructed to keep their eyes closed and remain relaxed. Subjects were instructed not to fall asleep. Each subject wore a fitted electrode cap (Electro-Cap International Inc., Eaton, OH) using the 19-channel montage as specified according to the 10–20 International system [FP1, FP2, F7, F3, Fz, F4, F8, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8, O1, O2]. The nose served as reference and the forehead was the ground electrode. Electrode impedances were always maintained below 5 kΩ. Electrooculogram (EOG) was recorded from electrodes placed supraorbitally and on the outer canthus of eye. Vertical and horizontal eye movements were monitored to perform ocular artifact correction. Electrical activity was amplified 10,000 times by Sensorium EPA-2 electrophysiology amplifiers (Charlotte, VT), with a bandpass between 0.02 Hz and 50 Hz and digitized on a Concurrent 5550 computer (Concurrent Computer Corp., Atlanta, GA). The sampling rate was 256 Hz, and the activity was recorded for 4.25 min.

Data Reduction and Analysis

Analysis of EEG was performed at SUNY. A continuous interval comprising 256 sec of EEG data was selected for analysis. Offline raw data were subjected to wavelet filtering and reconstruction to eliminate high and low frequencies (Bruce and Gao 1994; Strang and Nguyen 1996). The s12 wavelet was used to perform a 6-level analysis, and the output signal was reconstructed with levels d6 through d3. This procedure is roughly equivalent to applying a band pass filter with a range of 2–64 Hz to the data. Subsequently, eye movements were removed by use of a frequency domain method developed by Gasser (Gasser et al 1986, 1987). This method subtracts a portion of observed ocular activity from observed EEG to obtain the true EEG, based on the difference between the cross-spectral values of trials with high ocular activity and those with low ocular activity. Visual inspection of corrected data showed satisfactory artifact removal characteristics.

The data were subsequently software transformed into 22 bipolar derivations, analyzed in 254 overlapping 2-sec epochs by use of a Fourier transform, and windowed using a Hamming function to improve the accuracy of the spectral results (Hamming 1983). The resulting spectral densities (sampled at 0.5-Hz intervals) were aggregated into bands, divided by the bandwidth, and subsequently averaged across epochs. Absolute power spectra were then calculated from these values. Bipolar derivations were used in preference over monopolar derivations to improve the spatial resolution of the electrical sources (Nunez et al 1995,

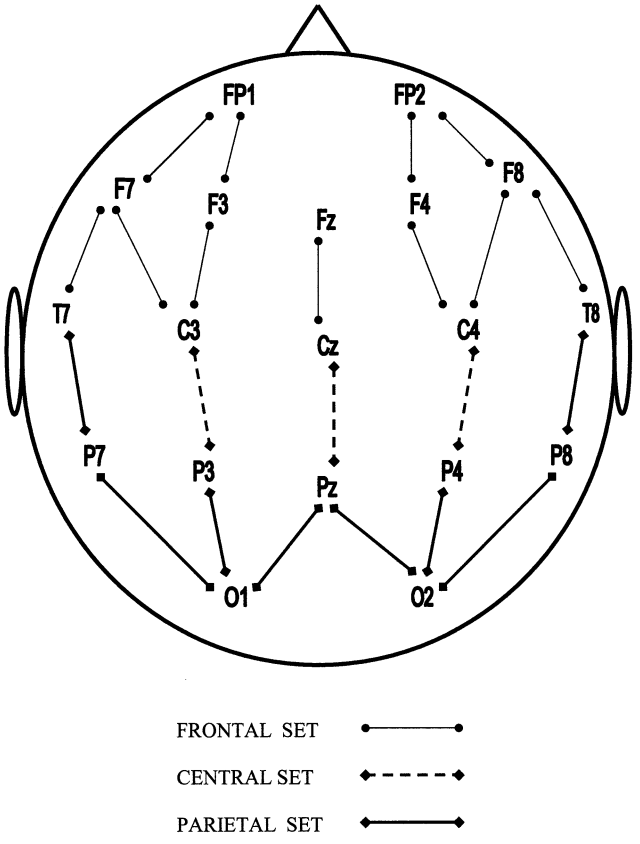

Figure 1. Topographical diagram of the electrode-pairs.

1997), especially because the 19-channel montage used in the study would not be appropriate for current source density analysis. Bipolar arrangements using close electrodes provide a higher pass spatial filter than is obtained with reference recordings. This method counteracts part of the smearing of cortical potentials and has also been shown to be more effective in capturing a greater amount of cerebral energy output than other referencing strategies (Cook et al 1998). A logarithmic transformation of the values was applied to the bipolar absolute power data to normalize their distributions. The normalized absolute Beta 1 (12.5–16 Hz), Beta 2 (16.5–20 Hz), and Beta 3 (20.5–28 Hz) band power data were analyzed for group differences using repeated measures of analyses of variance (RMANOVA) design (SAS, v6.11; SAS Institute, Inc., Cary, NC). Three regionwise groups of the electrode-pairs were determined, and the absolute beta power at each of these arrays was used as the dependent vector for comparisons between the two groups. The three sets were as follows (also see Figure 1):

1. Frontal: 11 electrode pairs (FP1-F3, FP2-F4, FP1-F7, FP2-F8, F3-C3, F4-C4, Fz-Cz, F7-T7, F7-C3, F8-T8, F8-C4)
2. Central: 3 electrode pairs (Cz-Pz, C3-P3, C4-P4)
3. Parietal: 8 electrode pairs (P7-T7, P7-O1, P8-T8, P8-O2, P3-O1, P4-O2, PZ-O1, PZ-O2)

The 22 electrode pairs were subjected to post hoc univariate tests to examine the topography of log power differences in detail.

The effect of clinical variables (total number of drinks in a typical week and recency of the last drink) and demographic (age) variables on the log beta power at all electrode pairs was examined in the sample of alcohol-dependent subjects using Pearson correlation matrix and regression analyses. To examine gender differences, the correlation and regression analyses were conducted separately on male and female subjects. Recency of last drink was used as a grouping variable (1: within 1 month [$n = 201$] and 2: >1 month [$n = 125$]). Gender was used as a covariate. The beta log power in the two subgroups of alcohol-dependent subjects was examined using multivariate design. Gender differences were examined by analyzing male and female populations separately for group differences using several RMANOVAs. The topographic distribution of the log power differences was examined using RMANOVAs on three region-wise electrode-pair groups (as defined earlier) and post hoc univariate analyses of each electrode pair.

Results

Subjects were age matched and were in the range of 18–50 years. Table 1 shows the genderwise description of demographic and clinical variables in the study sample. The mean typical weekly drink consumption was significantly different between the two groups. The table also lists the various co-morbid conditions and lifetime prevalence in the control subjects and alcoholics.

Beta Power Differences

The estimates of log-transformed mean absolute power in the Beta 1 (12.5–16 Hz), Beta 2 (16.5–20 Hz), and Beta 3 (20.5–28 Hz) bands were analyzed using RMANOVAs, with group and gender as the between-subjects factors and electrode location as the within-subjects factor. Four RMANOVAs were performed on the entire set of vertical electrode pairs and on three sets of regional arrays (Frontal, Central, and Parietal). The F values and significance levels for the group main effect are summarized in Table 2. The gender main effect was highly significant, but the interaction effect for group and gender was not significant for all three beta bands. In an attempt to examine the gender differences, multivariate analyses were performed for all three beta bands for male and female subjects separately.

Beta 1

Alcohol-dependent subjects showed higher beta amplitudes in contrast to control subjects at all electrode locations. The main effect for group [$F = 5.77$, $p < .017$] revealed a significant overall increase of beta power in the alcoholics (Table 2); however, regional analyses indicated the increased Beta 1 log power was significant over the central region [$F = 3.91$, $p < .048$] only. The mean log

Table 2. RMANOVA: *F* and *p* Values for Main Effect (Group) for the Total Alcoholic and Control Sample

	Beta 1 (12.5–16 Hz)		Beta 2 (16.5–20 Hz)		Beta 3 (20.5–28 Hz)	
Data set	*F*	*p*	*F*	*p*	*F*	*p*
All 22 pairs	5.77	.017	5.60	.018	4.03	.045
Frontal	2.53	.113	1.76	.185	3.23	.073
Central	3.91	.048	2.84	.092	2.41	.121
Parietal	3.20	.074	2.67	.103	2.11	.147

$n = 307$/group.
RMANOVA, repeated measures analysis of variance.

Beta 1 power values for selected electrode pairs and post hoc univariate significance levels are presented in Table 3. The increase in Beta 1 log power is prominent at fronto-central and parietal locations, with the most significant group difference occurring at Fz-Cz ($p < .009$).

Beta 2

Alcohol-dependent subjects showed higher beta amplitudes in contrast to control subjects at all electrode locations. The main effects for group revealed a significant overall increase of beta power in the alcoholics [$F = 5.60$, $p < .018$] (Table 2). The differences in Beta 2 log power in the three regions did not reach the significance level. Mean log Beta 2 power values for selected electrode pairs and significance levels of the post hoc univariate tests are presented in Table 3. In univariate analysis, the most highly significant group difference was seen for Fz-Cz ($p < .008$), F4-C4 ($p < .008$) and P7-O1 ($p < .007$) (Table 3).

Beta 3

The alcohol-dependent subjects showed higher beta amplitudes compared to control subjects at all electrode locations. The main effects for group for Beta 3 log power were significant at the overall level [$F = 4.03$, $p < .045$]. The mean log Beta 3 power values and univariate significance levels for selected electrode pairs is presented in Table 3. The univariate analysis indicates the differences to be most robust over some frontal and fronto-central regions, with the most significant differences occurring at F4-C4 ($p < .006$) and Fz-Cz ($p < .003$).

Gender and Beta Power Differences

BETA 1. Alcohol-dependent male subjects manifested higher Beta 1 power when compared to control male subjects at all electrode locations, as indicated by the significant main effect in the RMANOVA with all electrode-pairs [$F = 7.04$, $p = .008$] (Table 4). The differences, however, were more robust over the central and

Table 3. Mean Beta Log Power at Selected Electrode-Pairs and Significance Level of Post Hoc Tests for All Three Beta Bands in the Total Sample

	Beta 1 (12.5–16 Hz)			Beta 2 (16.5–20 Hz)			Beta 3 (20.5–28 Hz)		
Variable	Control subjects (Mean)	Alcoholics (Mean)	ANOVA (*p*)	Control subjects (Mean)	Alcoholics (Mean)	ANOVA (*p*)	Control subjects (Mean)	Alcoholics (Mean)	ANOVA (*p*)
FP2-F4	.07	.12	ns	.06	.12	ns	−.09	−.01	.044
FP1-F7	.08	.12	ns	.06	.13	.024	−.05	.02	.034
FP2-F8	.03	.06	ns	.04	.08	ns	−.07	.00	.035
F7-C3	.50	.56	.033	.042	.47	ns	.23	.27	ns
F8-C4	.51	.57	.018	.43	.49	.034	.22	.28	.033
F3-C3	.28	.35	.021	.18	.25	.018	−.03	.04	.018
F4-C4	.28	.36	.010	.18	.27	.008	−.03	.06	.006
Fz-Cz	.18	.27	.009	.07	.15	.008	−.13	−.03	.003
C3-P3	.41	.49	.017	.25	.33	.025	−.04	.00	ns
C4-P4	.44	.52	.014	.27	.35	.017	−.05	−.01	ns
T7-P7	.55	.61	.047	.44	.48	ns	.12	.14	ns
P7-O1	.41	.50	.014	.19	.28	.007	−.20	−.15	ns
P3-O1	.42	.50	.016	.26	.33	.040	−.14	−.10	ns
P4-O2	.40	.48	.012	.24	.32	.016	−.15	−.11	ns
Pz-O1	.68	.76	.014	.53	.59	ns	.14	.17	ns
Pz-O2	.66	.73	.038	.52	.56	ns	.14	.13	ns

$n = 307$/group.
ANOVA, analysis of variance.

Table 4. RMANOVA: *F* and *p* Values for Main Effect (Group) for Alcoholic and Control Male Subjects

	Beta 1 (12.5–16 Hz)		Beta 2 (16.5–20 Hz)		Beta 3 (20.5–28 Hz)	
Data set	*F*	*p*	*F*	*p*	*F*	*p*
All 22 pairs	7.04	.008	6.35	.012	5.55	.019
Frontal	5.11	.025	4.58	.033	6.45	.012
Central	7.22	.007	6.17	.014	3.53	.061
Parietal	6.88	.009	6.11	.014	2.88	.091

$n = 150$/group.
RMANOVA, repeated measures analysis of variance.

parietal regions, as indicated by the regional RMANOVAs [Central: $F = 7.22$, $p = .007$; Parietal: $F = 6.88$, $p = .009$] and univariate analyses for individual electrode pairs (Figure 2). Although female alcoholics had higher mean Beta 1 power in most electrode-pairs when compared to means from female control subjects, the difference was not robust enough to appear significant according to the RMANOVA and the univariate tests.

BETA 2. Alcohol-dependent male subjects had higher Beta 2 power when compared to control male subjects at all electrode locations, as indicated by the significant main effect in the RMANOVA with all electrode-pairs [$F = 6.35$, $p = .012$] (Table 4). The differences were more robust over central and parietal regions, as indicated by the regional RMANOVAs [Central: $F = 6.17$, $p = .014$; Parietal: $F = 6.11$, $p = .014$]. Univariate analyses for individual electrode pairs revealed significant differences at fronto-central, centro-parietal, and parietal regions (Figure 3). Female alcoholics had higher mean Beta 2 power in most electrode-pairs when compared to means from female control subjects, yet the difference was not robust enough to appear significant according to the RMANOVA and univariate tests. The increase of Beta 2 power in female alcoholics when compared to female control subjects at Fz-Cz location, however, is nearly significant on the univariate tests ($p = .066$).

BETA 3. Alcohol-dependent male subjects had higher Beta 3 power when compared to male control subjects at all electrode locations, as indicated by the means (Table 3) and a significant main effect in the RMANOVA with all electrode-pairs [$F = 5.55$, $p = .019$] (Table 4). The overall significance was mostly due to the frontal group of electrode pairs, as indicated by significant group main effect [Frontal: $F = 6.44$, $p = .012$]. Univariate analyses revealed significant differences at fronto-central and two centro-parietal electrode pairs only (Figure 4). Although female alcoholics had higher mean Beta 3 power in most electrode-pairs when compared to female control subjects, the difference was not robust enough to appear significant

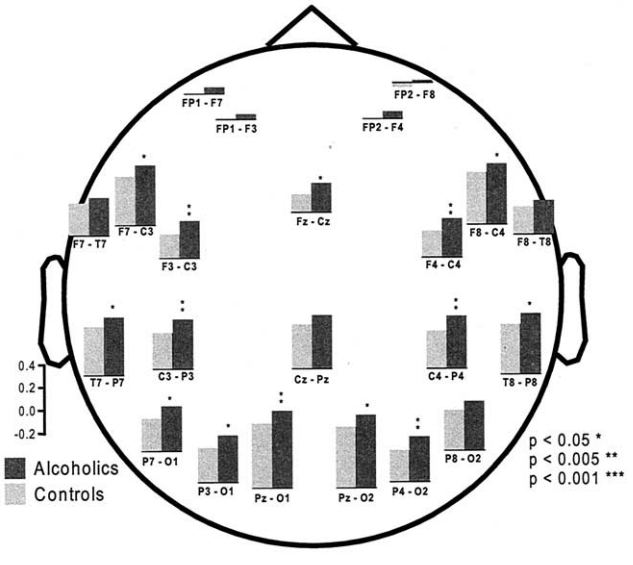

Figure 2. Mean Beta 1 log power in male subjects with post hoc significance levels.

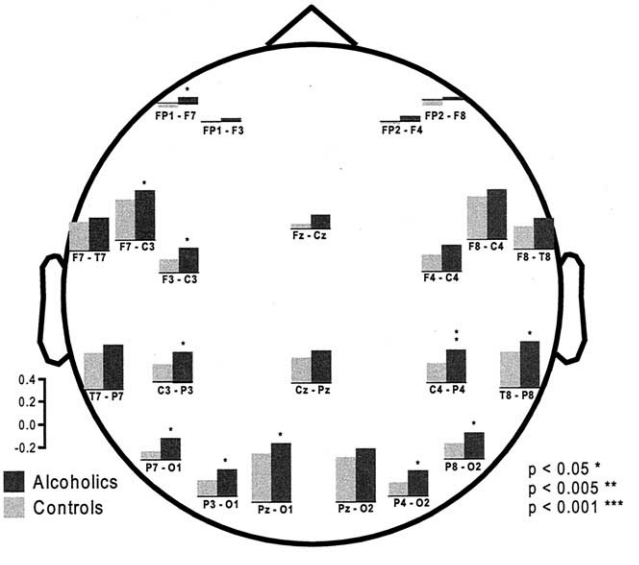

Figure 3. Mean Beta 2 log power in male subjects with post hoc significance levels. Logarithmic transformation of the data results in some negative values.

according to RMANOVA. The univariate tests however, reveal a significant increase of Beta 3 power in alcoholic females at the Fz-Cz location when compared to female control subjects ($p = .028$).

Effect of Age

The mean age for the two groups were not significantly different, because the sample was age matched (see Table 1). The linear model regression analysis of age and Beta 1, Beta 2, and Beta 3 log power produced a near-zero slope, suggesting very little influence of age on the variation of log beta power in the two groups. In addition, no gender differences were observed.

Effect of Clinical Variables

The two drinking measures used in the analyses were these:

1. Recency of drinking: the Recency variable did not differentiate between the two subgroups of the alcohol-dependent subjects for any of the three beta (Beta 1, Beta 2, and Beta 3) log power values for either gender.
2. Quantity of drinking: The total number of drinks consumed in a typical week (see Table 1). The Pearson's correlation matrix was computed for the total number of drinks consumed in a week versus log beta power at all electrode-pair locations. No significant correlations were obtained between the examined variables. No gender differences were noted.

Discussion

The present study demonstrated enhanced beta power in the resting EEG of alcoholics. This enhancement was not found to vary as a function of age or drinking variables (typical weekly drink total and recency of the last drink). Alcoholics show a consistent and significant increase in power at the Fz-Cz lead pair for all three beta bands. Male alcoholics have significantly higher beta power in all three beta bands (12.5–16 Hz, 16.5–20 Hz, 20.5–28 Hz). Although female alcoholics showed higher mean beta power in all three bands at most electrode pairs, the values did not reach significant levels in multivariate tests. Univariate analysis revealed significantly higher Beta 3 power at the Fz-Cz lead pair in female alcoholics.

Beta Power and Alcoholism

The finding in this study is consistent with existing reports of higher beta power in the resting EEG of alcoholics (Bauer 1994; Bauer et al 1997; Costa and Bauer 1997; Propping et al 1981); however, Propping et al (1981) reported elevation in number of beta waves only in female alcoholics and not in male alcoholics. The significant changes were observed at frontal and precentral regions. Bauer (1994) analyzed the entire beta band (13.2–27.6 Hz) in relapse-prone alcoholics and reported elevated beta power at the vertex (Cz) in those subjects. Winterer et al (1998) reported more desynchronized EEG over frontal areas in alcoholics prone to relapse. Pollock et al (1992) failed to find any differences in the beta band; however, their study consisted of a small sample of older, recovered alcoholics. The high variability of EEG data are, usually, a confounding factor in studies with small samples.

In our study we find a significant overall elevation in Beta 1, Beta 2, and Beta 3 log power in alcoholics. The analyses of the three regional electrode groups do not significantly differentiate between the two groups, thus indicating that the differences are more global and are strengthened by grouping all the locations. Hence, the univariate tests reveal the subtle regional differences. Post hoc univariate analyses showed the differences to be most significant at frontocentral, centroparietal, and parieto-occipital regions for Beta 1 and Beta 2, whereas Beta 3 log power elevation is largely frontocentral in topography. Yet it should be noted that for all beta bands, the most significant difference was at Fz-Cz. The results support existing studies that have reported a frontal focus of beta power change in alcoholics (Propping et al 1981; Winterer et al 1998), and nonalcoholic FHP men (Bauer and Hesselbrock 1993). A clear advantage of the present study is the large sample size. Owing to rather high variability in EEG datasets, subtle changes in the population characteristics cannot be delineated in small samples.

It could be argued that our sample has a significant proportion of alcoholics with cocaine and/or marijuana dependence that may have contributed to the results. Studies of chronic marijuana users (Struve et al 1998) have not reported beta power elevations but have reported an overall theta power increase. Studies examining quantitative EEG (qEEG) in cocaine-dependent patients have reported variable findings of enhanced alpha (Alper et al 1990; Prichep et al 1996), enhanced beta (Costa and Bauer 1997; Herning et al 1997; Noldy et al 1994; Pascual-Leone et al 1991), and enhanced alpha and beta with depressed delta (Roemer et al 1995). In a study examining EEG parameters in subjects with alcohol, cocaine, heroin, and dual substance abuse, Costa and Bauer (1997) report similar beta power elevations in alcohol-dependent and cocaine-dependent subjects when compared to normal control subjects but no significant beta power elevation in subjects dually dependent on alcohol and cocaine. An unknown premorbid variable, or a complex multivariate interchange between alcohol and drug use and other

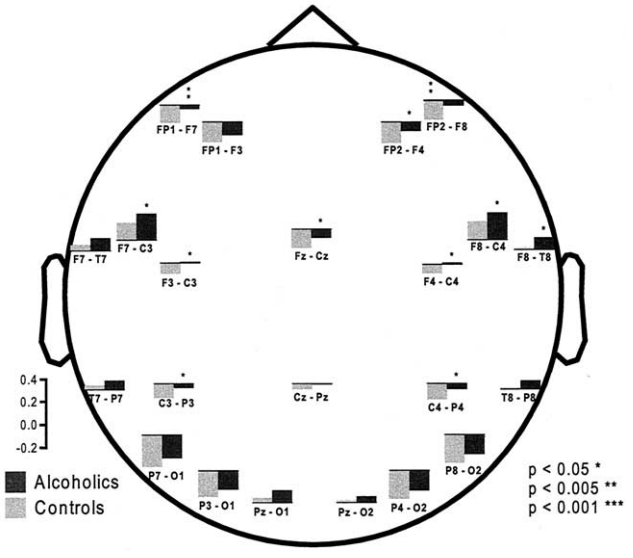

Figure 4. Mean Beta 3 log power in male subjects with post hoc significance levels. Logarithmic transformation of the data results in some negative values.

variables has been suggested as an explanation by some authors (Bauer 1994; Herning et al 1997). A recent paper (Bauer 2001) reporting elevated fast beta power (19.5–39.8 Hz) in relapse-prone alcoholics also highlights the importance of fast beta power over severity of illness, depression level, and childhood conduct problems, in predicting relapse in alcoholics. The author also suggests that the predictive capacity can be generalized across patients with histories of other substance abuse. Thus the elevated beta power we have observed in all three bands probably does not suggest a direct drug effect but rather a predisposition to substance use.

It should also be noted that disinhibitory behaviors, such as impulsivity, conduct disorder, failure to confirm to social norms, are commonly noted as externalizing traits in several clinical conditions (Gorenstein and Newman 1980). Studies have shown that alcohol-dependence and substance abuse are often comorbid with externalizing traits in children (Weinberg et al 1998) and adults (Wilens et al 1994); hence, all these conditions form a spectrum. Defining a stable electrophysiological marker in a heterogeneous population of alcoholics would greatly aid the study of alcoholism. The elevation of beta power in alcoholics could possibly be such a marker.

Beta and Gender Differences

In this study EEG beta power increases were significant in male alcoholics and did not reach significance in female alcoholics when compared to gender-matched control subjects. Although alcoholic females had significantly higher Beta 3 power at the fronto-central location, group differences were not significant in multivariate analyses. Only one study on resting EEG of alcoholics has assessed the issue of gender differences (Propping et al 1981), and they reported increased beta waves in female and not male subjects. The sample used in their study was much smaller (37 female subjects), and the mean age was slightly higher than our sample; however, the authors reported increases in beta waves in frontal and precentral regions, and this compares with our finding of increased Beta 3 at the fronto-central region in female alcoholics. Results from EEG studies on nonalcoholic subjects at risk for developing alcoholism highlight beta power increases in male subjects (Ehlers and Schuckit 1990; Gabrielli et al 1982; Pollock et al 1995). In this context it could be suggested that the higher beta power observed in male alcoholics reflects a difference that precedes alcohol abuse. Examining the EEG of the relatives of these alcoholics will shed more light on this issue.

Several reasons could explain the lack of strong findings in female alcoholics. Studies report differences in beta power between the various stages of the menstrual cycle (Kaneda et al 1997; Solis-Ortiz et al 1994). We did not include this aspect when analyzing the EEG data in females; hence it is possible that this factor may increase the variation in our data. Gender differences have been reported in abstinent cocaine abusers: female subjects show beta power ranges similar to control subjects, whereas cocaine-abusing men have a higher beta power compared to females and control subjects (King et al 2000). In our study population, 30.6% of the alcoholic subjects have associated cocaine dependence, and this might add to the variation in the female sample. Reports of gender differences in the EEG spectral profile indicate higher beta power in a population of normal and healthy female subjects when compared to normal, healthy, age-matched male subjects (Duffy et al 1993; Wada et al 1994). In the present study, mean power values for all three beta bands in both alcoholic and control female subjects are seen to be higher than the values for normal male subjects. Owing to high levels of resting beta power in EEG of female subjects, it is possible that there is a ceiling effect on further elevation of beta power by conditions that affect electrophysiological activity.

Neuronal Substrates of Beta

There is only a sparse literature that delineates neuronal substrates of beta rhythm recorded in scalp EEG. Rhythms recorded in beta and gamma ranges have been associated with attention, perception, and cognition (Farmer 1998; Singer 1993; Traub et al 1999). Several researchers using simulation and experimental methodologies have explored the mechanisms of neuronal fast oscillations (Kopell et al

2000; Whittington et al 2000a). These researchers suggest that beta and gamma band activity in the electroencephalogram are inhibition-based rhythms (Whittington et al 2000b). The authors report that the oscillations are produced by interactions in networks involving excitatory pyramidal cells and inhibitory interneurons. The mechanisms described, however, pertain to "active" beta, which is a subharmonic of gamma rhythm observed during mental activity.

Faulkner et al (1999) have described two kinds of beta rhythm in pyramidal cells—one that is a subharmonic of gamma rhythm and another that is not. The benzodiazepines and barbiturates produce a strong increase in EEG beta power, more marked in frontal regions. When used experimentally, benzodiazepines and barbiturates disrupt beta (excitatory pyramidal cell)/gamma (inhibitory interneuron) oscillations at the cellular level. Experiments have shown that the observed elevation in beta activity ("beta buzz") can be produced by pressure injection of glutamate or specific metabotropic glutamate agonists into a hippocampal slice (Traub et al 1996; Whittington et al 1996). In each case the observed beta rhythm occurs without an underlying gamma rhythm. The beta rhythm is produced by the slower pyramidal–interneuron network oscillations that are determined by GABAergic synaptic potentials in pyramidal cells and interneurons (Faulkner et al 1998). The synaptic potentials are larger with benzodiazepine and longer with barbiturate application, thus producing beta range oscillations in both pyramidal and interneuron cells (Faulkner et al 1999). Similarly, increases in glutamatergic drive to cortical neuronal networks could also contribute to the increased beta power observed. Strengthening the hypothesis for involvement of $GABA_A$ receptors in the beta frequencies of the human EEG is a recent study reporting a significant linkage and linkage disequilibrium between beta and a set of $GABA_A$ receptor genes (Porjesz et al, 2002).

Alcoholism, Frontal Pathology, and Beta Increase

Recent imaging studies have demonstrated significantly reduced levels of GABA-benzodiazepine (BDZ) receptors in alcohol-dependent individuals (Lingford-Hughes et al 1998) and in the cortex of type II alcoholics (Abi-Dargham et al 1998). A study by Behar et al (1999) also demonstrated reduced cortical GABA levels in detoxified alcoholics. Taber et al (2000) have explored the electrophysiological, structural, and biochemical evidence addressing the issue of cortical inhibition. The authors underscore the importance of GABAergic systems in the cause and effect of alcohol dependence. The reduction in the levels of GABA and its receptor possibly allows enhanced coupling between excitatory neurons (E–E coupling), thereby contributing to enhanced beta activity (Koppell et al 2000). It has been shown that alcohol affects the regulation of the NMDA (*N*-methyl-D-aspartate) receptor numbers in the central nervous system (Tsai and Coyle 1998). The NMDA is a fast acting glutamatergic receptor involved in excitatory transmission in the pyramidal cells. In addition, another positron emission tomography (PET) study suggested that alcohol dependence is associated with changes in neurons that contained $GABA_A$-BDZ receptors in the superior medial regions of the frontal lobes (Gilman et al 1996). In our study the most consistent increases in all three beta bands was noted in anterior leads (Fz-Cz, F4-C4, F3-C3, and F8-C4) indicating a possible frontal locus of pathology. A PET study also suggests that there is some evidence of the GABA-BZD receptor system impairment in individuals at risk for developing alcoholism (Volkow et al 1995). Our results coupled with the results of imaging studies suggest a possible association of frontal pathology in alcoholics with increased beta power in frontal regions.

In the model for understanding the neurophysiological basis of alcoholism proposed by Begleiter and Porjesz (1999), the importance of the balance of inhibition–excitation in maintaining cortical homeostasis is highlighted. They suggest that an inheritance of a general state of CNS disinhibition/hyperexcitability predisposes an individual to develop alcoholism. Consumption of alcohol temporarily alleviates this state of hyperexcitability but later exacerbates it. In the present study it is possible that the increased beta power observed is an index of a hyperexcitability that is produced by an excitation–inhibition imbalance that might exist in the alcoholic brain. In addition to this predisposition, it is possible that the increase in beta power observed has contributions from the exacerbated state of excitation–inhibition imbalance produced by prolonged alcohol use.

In conclusion, this study demonstrates that the elevation of all three bands of beta power is a strong feature of the resting EEG of chronic alcoholics. Male alcoholics manifest this difference more clearly than female alcoholics, perhaps owing to certain physiologic variables adding to the variability of the data in female alcoholics. The elevation of beta power in alcoholics has a largely anterior topography, especially in the higher frequency band (20–28 Hz). Further research in this area is necessary to determine if this elevation is a feature that becomes apparent during the development of alcoholism, hence being a "state"-related condition. Although there is some evidence that there is increased beta in individuals at risk, the beta power profile in the resting EEG of relatives of alcoholics needs to be more fully examined to assess if the beta power elevation is a "state"- or "trait"-related feature. The predictive capacity of increased beta power in differ-

entiating subjects predisposed to alcoholism also needs to be determined. Hence the beta power in the EEG of children of alcoholics, especially before alcohol exposure, needs to be examined.

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