0145-6008/03/2704-0607$03.00/0
Alcoholism: Clinical and Experimental Research

Vol. 27, No. 4
April 2003

Theta Power in the EEG of Alcoholics

Madhavi Rangaswamy, Bernice Porjesz, David B. Chorlian, Keewhan Choi, Kevin A. Jones, Kongming Wang, John Rohrbaugh, Sean O'Connor, Sam Kuperman, Theodore Reich, and Henri Begleiter

Background: In this study, the magnitude and spatial distribution of theta power in the resting EEG were examined to explore the changes in the neurophysiological status of the alcoholic brain. Some state- and trait-related issues of theta power increases in the EEG of alcoholics were also examined.

Methods: Absolute theta (3–7 Hz) power in eyes-closed EEGs of 307 alcohol-dependent subjects and 307 age- and gender-matched unaffected controls were compared by using a repeated-measures ANOVA for the entire region and three subregions (frontal, central, and parietal) separately. Supplementary to the main analysis, the effect of three clinical variables on absolute theta power was examined separately for each gender by using correlation and regression analyses. Gender differences in the theta log power difference between alcoholics and controls were explored by using regional repeated-measures ANOVA.

Results: Increased absolute theta power was seen in alcohol-dependent subjects at all scalp locations. The theta log power increase in male alcoholics was prominent at the central and parietal regions and in female alcoholics at the parietal region when compared with the respective matched controls. Correlation of drinking variables with log theta power exhibited no group-specific differences.

Conclusions: Increased tonic theta power in the EEG may reflect a deficiency in the information-processing capacity of the central nervous system in alcoholics. The theta power increase may also be an electrophysiological index of the imbalance in the excitation-inhibition homeostasis in the cortex. It is likely that the theta power increase is a trait-related phenomenon and is expressed to differing degrees in the two genders.

Key Words: Theta, EEG, Alcoholism, Absolute Power.

THE ELECTROENCEPHALOGRAM (EEG) has been used as an informative measure of the status of the alcoholic brain and the neurophysiological effects of chronic alcohol abuse and withdrawal. Early EEG studies of alcohol-dependent subjects were oriented toward the study of abnormal events, such as seizures, spikes, and high-voltage waves during the acute withdrawal and abstinence periods (Begleiter and Platz, 1972). Most studies concur that abnormalities in the EEG consist of the following: (a) severe pathologic changes, such as persistent arrhythmias, dysrhythmias, abnormal spiking, and paroxysmal high-voltage slow waves (Naitoh, 1973), or (b) other EEG disturbances, such as instability or disappearance of alpha rhythm, occurrence of increased low-voltage fast activity, and diffuse theta and delta waves. These studies report generalized slowing and reduction of alpha and increases in the slow (theta and delta range) and the fast (beta range) frequencies (Little and McAvoy, 1952). More frequent abnormalities in the EEG, especially in the temporal regions, along with increased diffuse theta activity (Arentsen and Sindrup, 1963), also have been reported. Comparisons of the more current studies with older studies have been limited owing to the use of qualitative versus quantitative approaches, the differences in the definition of "abnormality" in the EEG, and the wide individual differences in patients diagnosed as "alcoholic." Later studies have more specifically addressed state- and trait-related aspects of the electrophysiological changes observed, by analyzing the resting EEG in alcoholics and high-risk subjects and by acute studies with the high-risk population.

Studies of resting EEG in alcoholics are few. Propping et al. (1981) published an extensive study of the resting EEG in alcoholics and their relatives. The authors reported no differences in the EEG of male alcoholics when compared with age-matched controls; all statistically significant differences observed were seen in the female alcoholics. Theta waves occupied proportionally shorter durations of resting EEG in female alcoholics when compared with female controls, especially in the anterior and central location. In contrast, beta waves were present for proportionally longer durations in the EEG of female alcoholics when compared

From the Department of Psychiatry, State University of New York, Health Science Center at Brooklyn, New York (MR, BP, DBC, KW, KAJ, KC, HB); Department of Psychiatry, Institute of Psychiatric Research, Indiana University Medical Center, Indianapolis, Indiana (SO); University of Iowa Hospitals, Division of Child Psychiatry, Iowa City, Iowa (SK); Department of Psychiatry, Washington University, School of Medicine, St. Louis, Missouri (TR); and Washington University, Division of Family Studies, St. Louis, Missouri (JR).

Received for publication April 16, 2002; accepted January 13, 2003.
Supported by NIH Grant U10AA08403 from the NIAAA.

Reprint requests: Bernice Porjesz, PhD, Department of Psychiatry, Box 1203, SUNY, HSCB, 450 Clarkson Ave., Brooklyn, NY 11203; Fax: 718-270-4081; E-mail: bp@cns.hscbklyn.edu.

DOI: 10.1097/01.ALC.0000060523.95470.8F

with the female controls. The duration of alpha waves in the EEG was shorter in female alcoholics, but the difference was not statistically significant. The mean amplitude of alpha, beta, and theta bands was also examined, and no significant differences were noted. The relatives of male probands, who manifested poorly synchronized EEGs, had a profile similar to that of female alcoholics. However, the study did not report any statistical analyses on the overall population.

A qualitative study of resting EEG in chronic alcoholics by Johannesson et al. (1982) revealed a higher proportion of abnormal records in the youngest and oldest groups of alcoholics. The EEGs of the alcoholics showed increased diffuse theta and delta waves and medium-voltage spiking. They also showed a significant correlation of earlier onset of abuse with increased frequency of EEG abnormalities. Pollock et al. (1992) studied older recovered alcoholics (35–75 years) along with age-matched controls and found only theta band differences between groups. The differences were marked in the anterior regions of the scalp. The heterogeneity of the group studied did not affect the levels of significance. Costa and Bauer (1997) reported increased beta power in alcohol-dependent and cocaine-dependent subjects in their study comparing various substance-dependence categories. Bauer (1994) reported higher beta power at the vertex in the relapsers compared with the controls and abstainers. Another recent study focusing on aspects of abstinence (Winterer et al., 1998) reported a more desynchronized EEG in the frontal leads of relapsers. Thus, in the study of EEG characteristics in alcoholics, two points of focus emerge from existing studies: increased beta power and changes in the slower (theta) frequency band.

Several studies have examined the EEG in high-risk subjects, at resting condition and with an ethanol challenge, to determine which of the frequency changes observed are features that precede alcoholism (trait variable), are a consequence of drinking alcohol (state variable), or both. The studies of high-risk subjects have largely reported alpha and beta changes in the resting EEG and also in the EEG after ethanol challenge (Ehlers and Schuckit, 1990, 1991; Finn and Justus, 1999; Gabrielli et al., 1982; Pollock et al., 1995). Some studies found no baseline differences between low- and high-risk subjects (Cohen et al., 1991; Pollock et al., 1983). Acute studies using ethanol challenge have reported theta frequency band increases in addition to changes in alpha and beta bands (Ehlers et al., 1989; Lukas et al., 1986).

The findings from the existing studies on alcoholics and high-risk subjects have, however, been quite variable. Several factors may contribute to the variability, including (a) small sample sizes; (b) characteristics of the population, such as age (Johannesson et al., 1982), psychiatric comorbidity (Bauer and Hesselbrock, 1993), liver disease, nutritional status, and neurological status (Krauss and Neidermeyer, 1991; Spehr and Stemmler, 1985); and (c) differences in the quantitative and qualitative methods of analysis.

Our study examines the differences in the EEG spectrum of the alcoholics and unaffected control subjects. Each of the major frequency bands (theta, alpha, and beta) of the EEG has specific functional significance and varying distribution characteristics over the scalp (Neidermeyer, 1999). The differences between this sample of alcoholics and controls in the beta band frequencies have been reported earlier (Rangaswamy et al., 2002). In this article, we report the differences observed in the absolute power of the theta (3- to 7-Hz) band in the resting EEG of alcoholics in comparison to normal age- and sex-matched control subjects. We examined the magnitude of the difference in absolute power of the theta band (3–7 Hz) both globally and regionally, to assess the topographical differences between the groups. The relationship between absolute theta power and age was examined to assess whether the age relationship was different in the alcoholic and control groups. We also examined the effect of drinking variables on the theta absolute power to assess whether group differences were influenced by drinking variables per se (i.e., were state related).

METHODS

Subjects

Subjects were participants in the ongoing Collaborative Study on the Genetics of Alcoholism (COGA), a multisite national consortium designed to study the genetics of alcoholism. The collaborative sites are located at State University of New York 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 before recruitment into the study. The institutional review board at each site approved 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 and Porjesz, 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. Controls were not excluded on the basis of psychiatric illness or alcoholism, to obtain prevalence rates similar to those in the general population.

Subjects were also excluded from the neurophysiological assessment if they manifested uncorrected sensory deficits, had hepatic encephalopathy or cirrhosis of the liver, had significant head injury or seizures, had acute or chronic illness and were taking medication that affects or 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 subjects was picked 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).

Table 1. Sample Characteristics

Variable	Alcoholics		Controls	
	Male	Female	Male	Female
n	150	157	150	157
Age, years, mean (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 hr[a]	32.09	18.68	13.67	6.70
% Cocaine dependent—DSM-III-R	34	43	1.3	1.9
% Marijuana dependent—DSM-III-R	50	29.9	3.3	6.4
% Stimulant dependent—DSM-III-R	20.7	10.2	0	0.6
% Sedative dependent—DSM-III-R	10	8.3	0	0
% Lifetime depression—DSM-III-R	14	19.1	10.7	24.2
% Antisocial personality disorder—DSM-III-R	24	6.4	3.3	0

[a] One drink was defined as one shot glass of hard liquor, one glass of wine, or one bottle of beer; one drink equals approximately 9 g of absolute alcohol.

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 Co., Bronx, NY) and instructed to keep their eyes closed and to remain relaxed. Subjects were instructed not to fall asleep. Each subject wore a fitted electrode cap (Electro-Cap International Inc., Eaton, OH) with the 19-channel montage as specified according to the international 10-20 system (FP1, FP2, F7, F3, Fz, F4, F8, T7, C3, Cz, C4, T8, P7, P3, Pz, P4, P8, O1, and O2). The nose served as reference, and the forehead was the ground electrode. Electrode impedances were always maintained below 5 kΩ. Electro-oculogram was recorded from electrodes placed supraorbitally and at 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 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

EEG analysis was performed at State University of New York. A continuous interval comprising 256 sec of EEG data was selected for analysis. Off-line 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 six-level analysis, and the output signal was reconstructed with levels d6 through d3. This procedure is roughly equivalent to applying a bandpass filter with a range of 2 to 64 Hz to the data. Subsequently, eye movements were removed by use of a frequency domain method developed by Gasser et al. (1986, 1987). This method subtracts a portion of observed ocular activity from observed EEG to obtain the true EEG on the basis of 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 20 bipolar derivations, analyzed in 254 overlapping 2-sec epochs by use of a Fourier transform, and windowed by 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, 1995; Nunez et al., 1997), especially because the 19-channel montage used in the study would not be appropriate for current source density analysis. Bipolar arrangements with 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 more 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.

Statistical Analyses

Our objective was to compare the absolute power of the theta band (3–7 Hz) in the resting EEG between alcoholic and control subjects. Because it is well established that gender and age are significant confounders (i.e., covariates) for EEG and alcoholism, our study design is that of an age- and gender-matched case control study (case = alcoholics). In other words, for each case, we selected a control whose age (within 1 year) and gender were the same as the case's.

Primary Analyses. The normalized absolute theta (3- to 7-Hz) band power data in 20 electrode pairs were analyzed for group differences by using a repeated-measures ANOVA (RMANOVA) design (SAS, version 6.11, SAS Institute, Cary, NC), with absolute theta power (log) as the dependent variable and group (alcoholic/control) as the independent variable. RMANOVA of the theta power was performed in two stages: first globally, i.e., across all 20 electrode pairs, and then by regional RMANOVAs for the frontal, central, and parietal regions separately. The three regions comprised the following electrode pairs (Fig. 1).

1. Frontal: 11 electrode pairs (FP1/F3, FP2/F4, FP1/F7, FP2/F8, F3/C3, F4/C4, Fz/Cz, F7/C3, F8/C4, F7/T7, and F8/T8).
2. Central: 3 electrode pairs (Cz/Pz, C3/P3, and C4/P4).
3. Parietal: 6 electrode pairs (P7/O1, P8/O2, P3/O1, P4/O2, PZ/O1, and PZ/O2).

Secondary Analysis. We compared the theta log power between alcoholics and controls for each gender separately by using regional RMANOVAs for frontal, central, and parietal regions.

Supplementary Analyses. The effect of clinical variables (the total number of drinks in a typical week and the maximum number of drinks consumed in 24 hr) and demographic (age) variables on the log theta power at all electrode pairs was examined in the sample of alcohol-dependent subjects by using correlation analysis separately for each gender. The effect of the recency of drinking on log theta power was examined by using a multivariate design. The recency of the last drink was used as a grouping variable, and the alcohol-dependent subjects were sorted into five groups on the basis of when they had their last drink, viz., (1) within 2 weeks (n = 165), (2) 2 weeks to 1 month (n = 36), (3) 1 to 6 months (n = 64), (4) 6 months to 1 year (n = 13), and (5) more than 1 year (n = 48). The analysis was conducted separately for the two genders.

RESULTS

Subjects were age-matched and were in the range of 18 to 50 years. Table 1 summarizes the mean age of the male

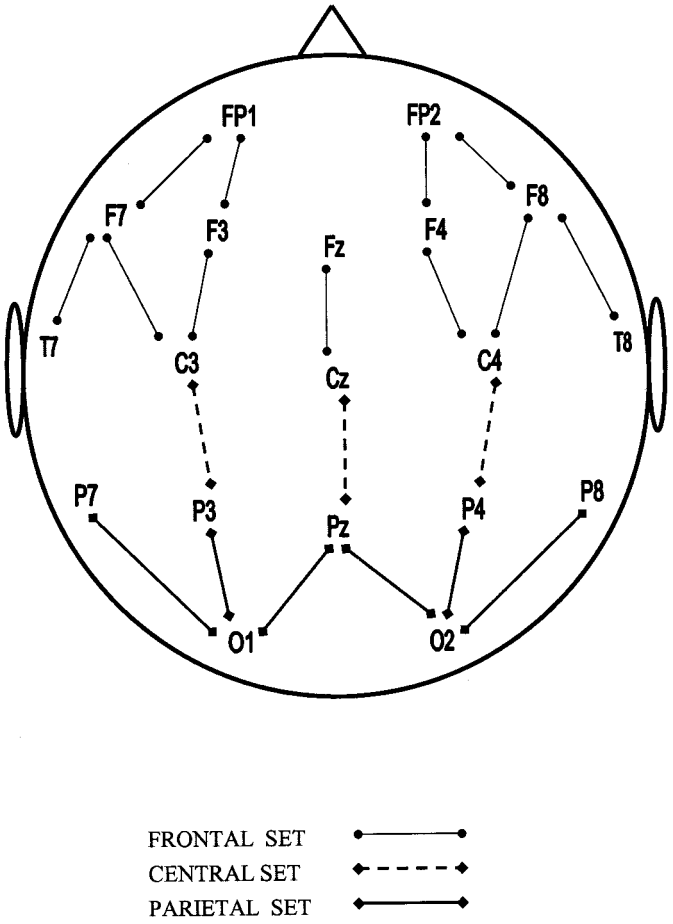

Fig. 1. Representation of the frontal, central, and parietal electrode pairs used in the log theta power analyses.

and female subjects in the study sample. The mean typical drink consumption per week was 1.74 drinks for the controls and 15.71 for the alcohol-dependent subjects (Table 1). The difference between the two groups was highly significant. The table also lists the various comorbid conditions and lifetime prevalence for both genders in controls and alcoholics.

Theta Power Differences

The estimates of log-transformed mean absolute power in the theta band (3–7 Hz) were analyzed by using RMANOVA, with group as the between-subjects factor and electrode location as the within-subjects factor. The analyses were performed on the entire set of vertical electrode pairs and three sets of regional arrays, viz., frontal, central, and parietal. The F values and significance levels for the main effects are summarized in Table 2.

The alcohol-dependent subjects showed higher theta amplitudes in contrast to the controls at all electrode locations, as is evident from the main group effect. The main effect for group was significant overall ($F = 8.86$; $p < 0.003$) and for the regional arrays: frontal ($F = 3.91$; $p < 0.048$), central ($F = 8.48$; $p < 0.004$), and parietal ($F = 13.56$; $p < 0.0003$) (Table 2).

Table 2. Results of the RMANOVA Analyses

	Main effect—group	
Dataset	*F*	*p* Value
All 22 pairs	8.86	0.003
Frontal	3.91	0.048
Central	8.48	0.004
Parietal	13.56	0.0003

Gender and Theta Power Differences

The difference in theta log power between alcoholics and controls (delta value) has been summarized in three histograms for the following regions: frontal (Fig. 2), central (Fig. 3), and parietal (Fig. 4). The differences were computed at each electrode pair and for each gender separately. We examined the difference in the mean log theta power of alcoholics and controls at frontal, central, and parietal regions separately for the two genders. In the supplementary regional analysis, significant differences in men were seen for the central ($p = 0.020$) and parietal ($p = 0.001$) regions and only for the parietal region ($p = 0.041$) in women (Table 4).

Effect of Clinical Variables

Three drinking measures were used in the analyses.

1. Recency of drinking:

The analysis was restricted to the alcohol-dependent subject sample. The recency variable did not differentiate theta band power between any of the five subgroups of subjects in either the multivariate ANOVA or post hoc univariate analyses for both men and women.

2. Quantity of drinking:

a. The total number of drinks consumed in a typical week (Table 1): the Pearson's correlation matrix was computed for the total number of drinks consumed in a week versus log theta power at all the electrode-pair locations. No significant correlations were obtained between the examined variables for men and women.
b. The maximum number of drinks consumed in a 24-hr period: the correlation matrix for this variable versus the log theta power values at all electrode pairs was computed. No significant correlations were observed between the maximum number of drinks and the log theta power value at any of the electrode pairs for both men and women.

DISCUSSION

In this study, we examined the resting eyes-closed EEG in alcohol-dependent and age-matched control subjects and

Table 3. Mean Log Theta Power at the Vertical Electrode Pairs

	Controls (n = 307)		Alcoholics (n = 307)	
Pair	Mean	SD	Mean	SD
FP1-F3	0.7279	0.3275	0.7587	0.3068
FP2-F4	0.6844	0.3146	0.7338	0.3348
FP1-F7	0.5962	0.3239	0.6347	0.3187
FP2-F8	0.5431	0.2919	0.5630	0.2859
F7-T7	0.5929	0.3054	0.6395	0.2949
F8-T8	0.5564	0.3033	0.6084	0.3013
F7-C3	0.9639	0.2850	1.0170	0.3101
F8-C4	0.9603	0.2826	1.0088	0.2869
F3-C3	0.6272	0.3599	0.6899	0.3285
F4-C4	0.6157	0.3440	0.6674	0.3346
Fz-Cz	0.7761	0.3582	0.8031	0.3457
Cz-Pz	0.8152	0.3764	0.8766	0.4170
C3-P3	0.6144	0.3804	0.6996	0.3676
C4-P4	0.6357	0.3606	0.7372	0.3719
P7-O1	0.5919	0.4542	0.7273	0.4330
P8-O2	0.6567	0.3798	0.7639	0.3890
P3-O1	0.6619	0.4232	0.7667	0.4045
P4/O2	0.6353	0.3771	0.7521	0.3894
Pz/O1	0.9287	0.4009	1.0238	0.4285
Pz/O2	0.9000	0.3987	1.0020	0.4221

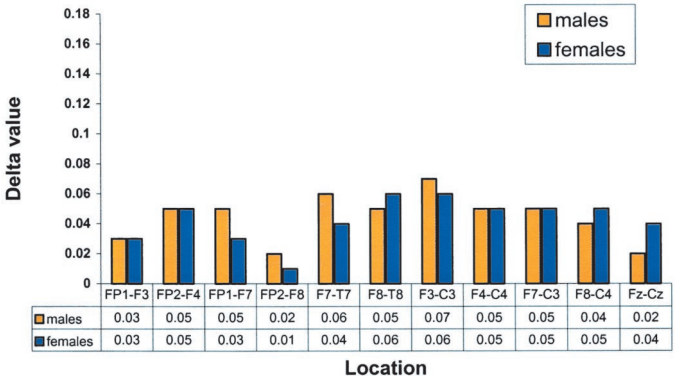

Fig. 2. Theta power differences between alcoholics and controls (delta) at frontal locations in men and women.

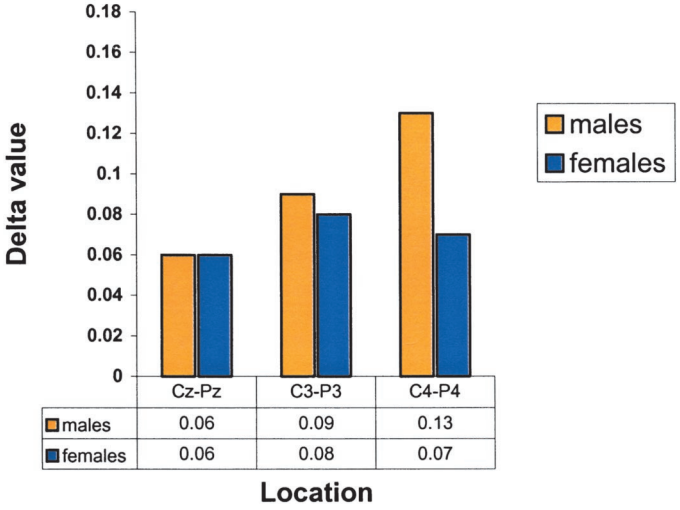

Fig. 3. Theta power differences between alcoholics and controls (delta) at central locations in men and women.

found increased absolute theta log power at all locations on the scalp. Correlation of drinking variables with log theta power exhibited no group-specific differences. Our study revealed similar differences in the EEG of alcohol-dependent male and female subjects when compared with respective age-matched control samples. Topographic differences were noted in the theta power increase in male and female alcoholics. The theta log power increase was significantly higher in male alcoholics at the central and parietal regions. Female alcoholics had higher theta log power in the parietal region only.

EEG and Alcoholism

The results of several studies that have examined the resting EEG of alcohol-dependent individuals reveal a specific pattern of change. The early studies (Arentsen and Sindrup, 1963; Little and McAvoy, 1952), using a largely qualitative approach, indicated the presence of a higher incidence of abnormalities in the EEG of alcoholics when compared with the control subjects. These studies also highlight a higher frequency of occurrence of abnormalities in the slow (delta and theta) and fast (beta) frequencies in the EEG of alcoholics. This observation was substantiated by later studies using improved quantitative methodology, which demonstrated significant differences in theta and beta bands. Differences in the beta band of resting EEG have been consistently reported in affected individuals (Bauer, 1994; Costa and Bauer, 1997; Propping et al., 1981; Rangaswamy et al., 2002; Winterer et al., 1998). With the exception of one study that reported longer durations of beta waves (Propping et al., 1981), other studies reported an increase in the power measure.

Studies reporting theta band changes are few and equivocal. One study reported a decrease in the duration of theta waves in female alcoholics (Propping et al., 1981), and

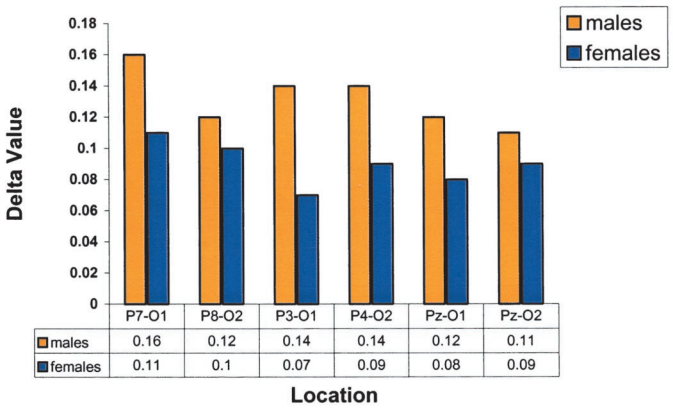

Fig. 4. Theta power differences between alcoholics and controls (delta) at parietal locations in men and women.

Table 4. Results of Supplementary RMANOVA

	men, main effect—group		women, main effect—group	
Dataset	*F*	*p* Value	*F*	*p* Value
Frontal	1.94	0.165	1.99	0.159
Central	5.47	0.020	3.30	0.070
Parietal	10.58	0.001	4.21	0.041

another study (Pollock et al., 1992) reported an increase in theta power in recovered alcoholics. The latter study included a heterogeneous sample of older alcohol-dependent subjects. Similar to our findings, these authors also found no relationship between the length of abstinence and theta measures in their sample of alcoholic subjects.

Alcoholism, as encountered in clinical settings, is a complex entity that involves a spectrum of coexisting addictive behaviors. Hence, we have attempted to characterize and establish the EEG profile in such a sample. The regional distribution of theta amplitudes seemed robust despite the heterogeneous composition of the alcohol-dependent sample. Apart from our study, there is only one other study reporting theta changes in the resting EEG of alcoholics (Pollock et al., 1992). In that study, the authors found that univariate analyses at each of the 28 individual scalp locations did not detect any significant increase in the theta power in the alcoholics. The differences were detected only when clusters of scalp sites were averaged into one variable. Using fast Fourier transform dipole approximation, Michel et al. (1992) deduced a posterior neural source for the theta rhythm in the resting eyes-closed EEG. The most significant increases of theta power in alcoholics, as noted in this study, have a central and/or posterior distribution on the scalp. This posterior neural source is possibly stronger and larger in the alcoholics when compared with the controls. In this study, the differences are robust at individual scalp sites, and the regional analyses indicate highly significant increases in theta power at central and posterior locations in alcohol-dependent subjects.

Gender Differences and Theta

The male alcoholic subjects demonstrate a strong group difference in the central and parietal regions, whereas the female alcoholics have a more posterior topography of theta power increase when compared with their respective matched controls. Ours is one of the few studies reporting the gender differences in theta power profile in a large sample of alcoholics. Only one earlier study has examined the gender differences in the EEG spectrum of the alcoholics. Propping et al. (1981) reported a decreased duration of theta waves in female alcoholics when compared with the age-matched controls in the anterior/central locations. The authors observed no differences in the male alcoholics. Pollock et al. (1991) reported increased theta amplitude in a sample of alcoholics comprising both genders. The sample, however, was predominantly male, and only 3% of the individuals were women. Our results demonstrate very strong gender differences in the theta log power increase in alcoholics (Figs. 2–4). It is possible that the theta system in the male alcoholics is more vulnerable than in female alcoholics.

Theta Power Increase—State or Trait?

The changes observed in the EEG of alcohol-dependent individuals are indicative of an altered neurophysiological condition in these individuals, reflected in the increase of tonic theta power in the resting state. The cause of the alteration, however, may be state or trait related.

The existing studies of the resting EEG of high-risk subjects have not reported any theta power changes, although they do report alpha and beta band changes in high-risk subjects (Bauer and Hesselbrock, 1993; Finn and Justus, 1999; Gabrielli et al., 1982; Pollock et al., 1995). One study examined the different EEG bands after the administration of alcohol. The authors reported increases in theta power in proportion to increasing blood alcohol content (Lukas et al., 1986). The authors suggest that this progression of increased theta activity may have been perceived as slowing of alpha in the earlier studies. Ehlers et al. (1989) also found a highly significant increase in both theta and low alpha band power 90 min after ethanol consumption. It is possible that the increases of theta produced by the acute administration of alcohol that is observed in healthy individuals subsequently evolve into a more pervasive increase in theta power in the resting EEG of chronic alcoholics after prolonged exposure. This hypothesis would suggest that the theta increase might be a state marker. However, in our study, we did examine three drinking variables—total drinks in a typical week, maximum number of drinks in a 24-hr period, and recency of the last drink. The drinking variables do not seem to influence the theta power profile, as indicated by the results of correlation and linear regression analysis.

The length of abstinence, as indexed by the recency of the last drink, did not affect the theta power difference in

this study sample. These results are similar to the findings of the study by Pollock et al. (1995), and we conclude that the alteration observed in the resting EEG of the alcohol-dependent subjects is not acute but of a more chronic nature. The lack of correlation of the increased theta power with drinking variables, however, does not support the hypothesis that this change is a direct consequence of alcohol consumption. We have examined the data and found a lack of linear relationship between the drinking variables and theta power. The possibility of a nonlinear relationship between the variables examined needs to be assessed to rule out any contribution of drinking variables to the absolute theta power profile. Another limitation encountered in this context exists owing to the subjective nature of acquiring information on the drinking variables. Because our estimates of the quantity of alcohol consumed come from subjective self-reports, the measures obtained need to be interpreted with caution. To explore the possibility that this increased absolute theta power is a trait-related change, the EEGs of individuals at risk need to be examined.

Tonic and Phasic Theta and Alcoholism

Posterior slow activity in the theta range constitutes an important aspect of EEG maturation from childhood to adolescence and early adulthood, continuing until the third decade (Neidermeyer, 1999). The normal adult waking record contains very low theta power, and increases in theta have been reported in several neurological states. An increase of theta rhythm has been seen in altered neurophysiological states of the brain, such as the transition from wakefulness to sleep (Tanaka et al., 2000), as well as in altered cholinergic functioning states, such as Alzheimer's disease (Huang et al., 2000) and aging (Neidermeyer, 1999). Slow EEG activity (theta and delta) has been well correlated with cholinergic activity and central cholinergic pathways (Steriade et al., 1990). In vitro studies (McCormick and Prince, 1986) have revealed that the mode of action of acetylcholine may either inhibit or excite cortical pyramidal neurons. The production of inhibition results from excitation of the intrinsic inhibitory neurons in the cortex.

The changes in the oscillatory components of the EEG have been described as being phasic or tonic, and the two differ in the mode of generation and their functional implications (Klimesch, 1999). Phasic changes are event related and occur at a rapid rate, whereas the tonic changes are not under volitional control and occur over the life cycle in response to circadian rhythms, fatigue, neurological conditions, and so on. Klimesch (1999), in an extensive review, described the tonic and phasic theta in the human EEG as behaving differently with respect to cognitive performance. Phasic theta, as observed in response to tasks with increasing memory load (Gevins et al., 1998), increases with increasing cognitive performance and decreases with decreasing performance. Tonic theta, as assessed under conditions of aging, sleep, and neurological conditions (Besthorn et al., 1997; Chiaramonti et al., 1997; Corsi-Cabrera et al., 1992; Hartikainen et al., 1992; Neidermeyer, 1999), decreases with increasing cognitive activity and increases with decreasing cognitive activity. Tonic theta changes appearing as increases in broadband synchronization possibly reflect a state in which the ability to encode new information is reduced or even blocked (Klimesch, 1999).

The theta power increase observed in the alcoholics found in this study shows a topographic distribution similar to that seen for tonic theta. Phasic theta topography, however, has a distinctly frontal and midline distribution (Gevins et al., 1998). Increased tonic theta in alcoholics may reflect the impaired information processing that has been observed in these subjects. This idea is strongly supported by results from our laboratory on a mental calculation task. In alcoholics performing a mental calculation task, the evoked frontal midline theta is lower than the control subjects (S. Suresh, unpublished data, 2003). Hence, there is strong evidence of impairment in both tonic and phasic theta in an alcoholic brain. The profile of cognitive and neurophysiological impairments in alcoholics has been well documented (Begleiter and Porjesz, 1995). P300 is a well established electrophysiological index of cognitive functioning (Polich and Kok, 1995). Low-voltage P3 components are characteristically observed in alcoholics and individuals at risk for developing alcoholism. These P300 deficits observed in alcoholics and the individuals at risk reveal an undifferentiated mode of responding to target and nontarget stimuli, suggesting an inability to use the available information (Porjesz and Begleiter, 1995, 1996, 1997). This inefficiency in brain processing possibly arises out of increased central nervous system hyperexcitability resulting from a reduction in inhibitory processes (Begleiter and Porjesz, 1999). Başar et al. (1998) demonstrated an inverse relationship between spontaneous prestimulus theta activity and the amplitude of the visual evoked potentials. Lower prestimulus theta activity resulted in larger amplitudes of N100/P200. P300 activity, especially in the hippocampus, manifests as theta enhancement or resonance phenomena in the theta frequency range (Başar-Eroglu et al., 1991a,b). A recent report examining the genetic correlation between P300 and the EEG spectrum suggests that a substantial proportion of genetic influences on P300 amplitude can be explained by the strong heritability of slow EEG rhythms contributing to P300 (Anokhin et al., 2001). We speculate that the low P300 reported in alcoholics and the high theta power in the resting EEG of the alcoholics seen in this study could reflect different aspects of the same cognitive dysfunctional state.

Alcoholism and Central Nervous System Hyperexcitability Model

As mentioned previously, the possibility of cholinergic influences on an increase of theta power cannot be ruled out. Neurochemically, the role of cholinergic (Hammond et al., 1987) and noradrenergic (Pineda et al., 1989) systems in the generation of the P300 have been clearly established in animal studies. There is compelling evidence (Porjesz et al., 1998) to support the candidacy of the amplitude of the visual P300 as a phenotypical marker for the predisposition to alcoholism. 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. The authors suggest that an inheritance of a general state of central nervous system disinhibition/hyperexcitability predisposes an individual to develop alcoholism. Consumption of alcohol alleviates this state of hyperexcitability, although temporarily. In this study, it is possible that the increased theta power observed is an index of a physiologic adaptation, providing a possible regulation of the excitation-inhibition imbalance that might exist in the alcoholic brain. This hypothesis is supported by two studies of the acute effects of alcohol on the EEG of healthy male subjects (Ehlers et al., 1989; Lukas et al., 1986). Both studies have shown an increase in theta power in the EEG of normal male subjects after consumption of ethanol.

In conclusion, this study shows the increase of theta power to be a strong feature of the resting EEG of chronic alcoholics. Further research in this area is necessary to examine whether the theta power increase is a feature that becomes apparent during developing alcoholism and, hence, is a state-related condition. The theta profile in the resting EEG of the relatives of alcoholics also needs to be examined to address the issue of theta increases being a state- or trait-related feature. The predictive capacity of increased theta power in differentiating subjects predisposed to alcoholism also needs to be determined. Hence, the theta power in the EEG of children of alcoholics, especially before alcohol exposure, needs to be examined.

ACKNOWLEDGMENTS

The Collaborative Study on the Genetics of Alcoholism (COGA) (H. Begleiter, State University of New York Health Sciences Center at Brooklyn Principal investigator, T. Reich, Washington University, Co-Principal Investigator includes nine different centers where data collection, analysis, and storage take place. The nine sites and Principal Investigators and Co-Investigators are: Howard University (R. Taylor); Indiana University (H. Edenberg, J. Nurnberger Jr., P.M. Conneally, T. Foroud); Rutgers University (J. Tischfield); Southwest Foundation (L. Almasy); State University of New York Health Sciences Center at Brooklyn (B. Porjesz, H. Begleiter); University of California at San Diego (M. Schuckit); University of Connecticut (V. Hesselbrock); University of Iowa (R. Crowe, S. Kuperman); Washington University in St. Louis (T. Reich, C.R. Cloninger, J. Rice, A. Goate). Lisa Neuhold serves as the NIAAA Staff Collaborator. The superlative assistance of Arthur Stimus, Aquanette Sass, Marty Krakowsky, Ed Babington, Sandi Watson, Vladimir Kotlyarevsky, Elizabeth Iskander, Marc Ostrega, and Sergio Valentini on this project is gratefully acknowledged.

REFERENCES

Anokhin AP, van Baal GC, van Beijsterveldt CE, de Geus EJ, Grant J, Boomsma DI (2001) Genetic correlation between the P300 event-related brain potential and the EEG power spectrum. Behav Genet 31:545–554.

Arentsen K, Sindrup E (1963) Electroencephalographic investigation of alcoholics. Acta Psychiatr Scand 39:371–383.

Başar E, Rahn E, Demiralp T, Schürmann M (1998) Spontaneous EEG theta activity controls frontal visual evoked potential amplitudes. Electroencephalogr Clin Neurophysiol 108:101–109.

Başar-Eroglu C, Başar E, Schmielau F (1991a) P300 in freely moving cats with intracranial electrodes. Int J Neurosci 60:239–248.

Başar-Eroglu C, Schmielau F, Schramm U, Schult J (1991b) P300 response of hippocampus analyses by means of multi-electrodes in cats. Int J Neurosci 60:239–248.

Bauer L (1994) Electroencephalographic and autonomic predictors of relapse in alcohol-dependent patients. Alcohol Clin Exp Res 18:755–760.

Bauer LO, Hesselbrock VM (1993) EEG, autonomic and subjective correlates of the risk for alcoholism. J Stud Alcohol 54:577–589.

Begleiter H, Platz A (1972) The effects of alcohol on the central nervous system, in *The Biology of Alcoholism, Vol 2: Physiology and Behaviour* (Kissin B, Begleiter H eds), pp 293–343. Plenum Press, New York.

Begleiter H, Porjesz B (1995) Event-related potentials and cognitive function in alcoholism. Alcohol Health Res World 19:108–112.

Begleiter H, Porjesz B (1999) What is inherited in the predisposition toward alcoholism? A proposed model. Alcohol Clin Exp Res 23:1125–1135.

Besthorn C, Zerfass R, Geiger-Kabisch C, Sattel H, Daniel S, Schreiter-Gasser U, Forstl H (1997) Discrimination of Alzheimer's disease and normal aging by EEG data. Electroencephalogr Clin Neurophysiol 103:241–248.

Bruce A, Gao H (1994) *S+ Wavelets User's Manual.* Mathsoft Inc., Seattle, WA.

Chiaramonti R, Muscas GC, Paganini M, Muller TJ, Fallgatter AJ, Versari A, Strik WK (1997) Correlations of topographical EEG features with clinical severity in mild and moderate dementia of Alzheimer type. Neuropsychobiology 36:153–158.

Cohen HL, Porjesz B, Begleiter H (1991) EEG characteristics in males at risk for alcoholism. Alcohol Clin Exp Res 15:858–861.

Cook IA, O'Hara R, Uijtdehaage SH, Mandelkern M, Leuchter AF (1998) Assessing the accuracy of topographic EEG mapping for determining local brain function. Electroencephalogr Clin Neurophysiol 107: 408–414.

Corsi-Cabrera M, Ramos J, Arce C, Guevara MA, Ponce-de Leon M, Lorenzo I (1992) Changes in the waking EEG as a consequence of sleep and sleep deprivation. Sleep 15:550–555.

Costa L, Bauer L (1997) Quantitative electroencephalographic differences associated with alcohol, cocaine, heroin and dual-substance dependence. Drug Alcohol Depend 46:87–93.

Ehlers CL, Schuckit MA (1990) EEG fast frequency activity in the sons of alcoholics. Biol Psychiatry 27:631–641.

Ehlers CL, Schuckit MA (1991) Evaluation of EEG alpha activity in sons of alcoholics. Neuropsychopharmacology 4:199–205.

Ehlers CL, Wall TL, Schuckit MA (1989) EEG spectral characteristics following ethanol administration in young men. Electroencephalogr Clin Neurophysiol 73:179–187.

Finn PR, Justus A (1999) Reduced EEG alpha power in the male and female offspring of alcoholics. Alcohol Clin Exp Res 23:256–262.

Gabrielli WF, Mednik SA, Volavka J, Pollock VE, Schulsinger F, Itil TM (1982) Electroencephalograms in children of alcoholic fathers. Psychophysiology 19:404–407.

Gasser T, Sroka L, Mocks J (1986) The correction of EOG artifacts by frequency dependent and frequency independent methods. Psychophysiology 23:704–712.

Gasser T, Sroka L, Mocks J (1987) The transfer of EOG activity into the EEG for eyes open and closed. Electroencephalogr Clin Neurophysiol 61:181–193.

Gevins A, Smith ME, Leong H, McEvoy L, Whitfield S, Du R, Rush G (1998) Monitoring working memory load during computer-based tasks with EEG pattern recognition methods. Hum Factors 40:79–91.

Hamming R (1983) *Digital Filters.* Prentice-Hall, Englewood Cliffs, NJ.

Hammond EJ, Meador KJ, Aung-Din R, Wilder BJ (1987) Cholinergic modulation of human P3 event-related potentials. Neurology 37:346–350.

Hartikainen P, Soininen H, Partanen J, Helkala EL, Riekkinen P (1992) Aging and spectral analysis of EEG in normal subjects: a link to memory and CSF AChE. Acta Neurol Scand 86:148–155.

Huang C, Wahlund L-O, Dierks T, Julin P, Winblad B, Jelic V (2000) Discrimination of Alzheimer's disease and mild cognitive impairment by equivalent EEG sources: a cross-sectional and longitudinal study. Clin Neurophysiol 111:1961–1967.

Johannesson G, Berglund M, Ingvar DH (1982) EEG abnormalities in chronic alcoholism related to age. Acta Psychiatr Scand 65:148–157.

Klimesch W (1999) EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. Brain Res Brain Res Rev 29:169–195.

Krauss GL, Neidermeyer E (1991) Electroencephalogram and seizures in chronic alcoholism. Electroencephalogr Clin Neurophysiol 78:97–104.

Little SC, McAvoy M (1952) Electroencephalographic studies in chronic alcoholism. Q J Stud Alcohol 13:9–15.

Lukas SE, Mendelson JH, Benedikt RA, Jones B (1986) EEG alpha activity increases during transient episodes of ethanol-induced euphoria. Pharmacol Biochem Behav 25:889–895.

McCormick DA, Prince DA (1986) Mechanisms of action of acetylcholine in the guinea-pig cerebral cortex in vitro. J Physiol 375:169–194.

Michel CM, Lehmann D, Henggeler B, Brandeis D (1992) Localization of the sources of EEG delta, theta, alpha and beta frequency bands using the FFT dipole approximation. Electroencephalogr Clin Neurophysiol 82:38–44.

Naitoh P (1973) The value of electroencephalography in alcoholism. Ann NY Acad Sci 215:303–320.

Neidermeyer E (1999) The normal EEG of the waking adult, in *Electroencephalography: Basic Principles, Clinical Applications, and Related Fields* (Neidermeyer E, Lopes da Silva eds), 4th ed, pp 149–173. Williams & Wilkins, Baltimore.

Nunez PL (1995) Quantitative states of neocortex, in *Neocortical Dynamics and Human EEG Rhythms* (Nunez PL ed), pp 3–67. Oxford University Press, New York.

Nunez PL, Srinivasan R, Westdorp AF, Wijesinghe RS, Tucker DM, Silberstein RB, Cadusch PJ (1997) EEG coherency. I: Statistics, reference electrode, volume conduction, Laplacians, cortical imaging, and interpretation at multiple scales. Electroencephalogr Clin Neurophysiol 103:499–515.

Pineda JA, Foote SL, Neville HJ (1989) Effects of locus coeruleus lesions on auditory, long latency, event related potentials in monkey. J Neurosci 9:81–93.

Polich J, Kok A (1995) Cognitive and biological determinants of P300: an integrative review. Biol Psychol 41:103–146.

Pollock VE, Earleywine M, Gabrielli WF (1995) Personality and EEG beta in older adults with alcoholic relatives. Alcohol Clin Exp Res 19:37–43.

Pollock VE, Schneider L, Lyness S (1991) Reliability of topographic quantitative EEG amplitude in healthy late middle aged and elderly subjects. Electroencephalogr Clin Neurophysiol 79:20–26.

Pollock VE, Schneider LS, Zemaksky MF, Gleason RP, Pawluczyk S (1992) Topographic quantitative EEG amplitude in recovered alcoholics. Psychiatry Res 45:25–32.

Pollock VE, Volavka J, Goodwin DW, Mednick SA, Gabrielli WF, Knop J, Schulsinger F (1983) The EEG after alcohol administration in men at risk for alcoholism. Arch Gen Psychiatry 40:857–861.

Porjesz B, Begleiter H (1995) Event related potentials and cognitive function in alcoholism. Alcohol Health Res World 19:108–112.

Porjesz B, Begleiter H (1996) Effects of alcohol on electrophysiological activity of the brain, in *Alcohol and Alcoholism, Vol 2: The Pharmacology of Alcohol and Alcohol Dependence* (Begleiter H, Kissin B eds), pp 207–247. Oxford University Press, New York.

Porjesz B, Begleiter H (1997) Event related potentials in COA'S. Alcohol Health Res World 21:236–240.

Porjesz B, Begleiter H, Reich T, Van Eerdewegh P, Edenberg HJ, Foroud T, Goate A, Litke A, Chorlian DB, Stimus A, Rice J, Blangero J, Almasy L, Sorbell J, Bauer LO, Kuperman S, O'Connor SJ, Rohrbaugh J (1998) Amplitude of visual P3 event-related potential as a phenotypic marker for a predisposition to alcoholism: preliminary results from the COGA project. Collaborative Study on the Genetics of Alcoholism. Alcohol Clin Exp Res 22:1317–1323.

Propping P, Kruger J, Mark N (1981) Genetic disposition to alcoholism. An EEG study in alcoholics and their relatives. Hum Genet 59:51–59.

Rangaswamy M, Porjesz B, Chorlian DB, Wang K, Jones KA, Bauer LO, Rohrbaugh J, O'Connor SJ, Kuperman S, Reich T, Begleiter H (2002) Beta power in the EEG of alcoholics. Biol Psychiatry 51:831–842.

Spehr W, Stemmler G (1985) Postalcoholic diseases: diagnostic relevance of computerized EEG. Electroencephalogr Clin Neurophysiol 60:106–114.

Steriade M, Gloor P, Llinas R, Lopes da Silva F, Mesulam M (1990) Basic mechanisms of cerebral rhythmic activities. Electroencephalogr Clin Neurophysiol 76:481–508.

Strang G, Nguyen T (1996) *Wavelets and Filter Banks*. Wellesley-Cambridge, Wellesley, MA.

Tanaka H, Hayashi M, Hori T (2000) Topographical characteristics of slow wave activities during the transition from wakefulness to sleep. Clin Neurophysiol 111:417–427.

Winterer G, Klöppel B, Heinz A, Ziller M, Dufeu P, Schmidt LG, Herrmann WM (1998) Quantitative EEG (QEEG) predicts relapse in patients with chronic alcoholism and points to a frontally pronounced cerebral disturbance. Psychiatr Res 78: 101–113.