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Complexity Changes of the EEG Induced by Alcohol Cue Exposure in Alcoholics and Social Drinkers

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Background: An understanding of the neurophysiological mechanisms underlying alcohol craving is important in the effective treatment of alcohol dependence. The aim of this study was to examine the utility of the electroencephalogram (EEG) to measure the changes in electrical brain activity of alcoholics when exposed to alcohol-specific cues.

Methods: Fifteen adult alcoholic subjects (four women) with a mean age of 35 (SD = 4.5) and 10 healthy social drinking controls (three women) with a mean age of 34 (SD = 5.6) were recruited. Subjects were serially rated for alcohol craving after presentations of pictures of control nonalcoholic and alcohol beverages. After the picture presentation, the EEG was recorded (16,384 data points for each epoch) with eyes closed. The dimensional complexity (D_2) was estimated as a measure of complexity of the EEG.

Results: Alcoholic subjects exhibited a significant increase in the D_2 values of the EEG in frontal (F_3, F_4), right posterior temporal (T_6), and occipital (O_1, O_2) regions after viewing alcohol cues compared with viewing other beverage cues. These results indicate that more complex (or higher) cortical activity is induced over specific brain regions of alcoholic subjects by alcohol-specific cues. Changes in subscale of alcohol craving between nonalcoholic and alcohol pictures were correlated with changes in D_2 values in the left frontal (F_3) region in alcoholic subjects.

Conclusions: These findings suggest that, when subjects are exposed to alcohol cues, changes in the EEG complexity are induced in frontal, right posterior temporal, and occipital areas, which may be key brain structures for alcohol craving. In addition, nonlinear measures like the D_2 are useful in evaluating alcohol cue-induced brain activity from the EEG.

Key Words: Alcohol Craving, Complexity, EEG, Alcohol Cue Exposure.

ONE OF THE major problems in the treatment of alcohol dependence is the propensity for relapse to drinking (Little, 1999; Ludwig, 1986). Such relapse has been reported in up to 90% of alcoholics during the 1 to 2 year period after therapeutic treatment (McKenna et al., 1996; Naranjo and Kadlec, 1991). High levels of craving for alcohol are associated with this increased probability of relapse (Anton, 1996). It is conventionally assumed that craving operates as a mediating variable that is responsible for the maintenance of all alcohol use in the ongoing alcoholic and that provides the necessary trigger for relapse in the alcoholic attempting to remain sober. Although craving is not central to the alcohol use of alcoholics, it serves as a cognitive marker of process that is associated with alcohol seeking and use (Tiffany and Conklin, 2000).

The causes of an increase in alcohol craving are thought to be 3-fold: sociopsychological elements such as frequent exposure to alcohol, external stress, anxiety, and depression (Childress et al., 1993); alcohol tolerance and withdrawal symptoms induced by long-term drinking (Koob and LeMoal, 1997); and biological elements through the actions of neurotransmitters including serotonin and β-endorphin (Kalivas et al., 1998; Koob and Roberts, 1999). Yet, the precise pathophysiological mechanism by which these elements induce alcohol craving in alcoholics is not clear. A better understanding of the neural mechanisms underlying craving is important in the development of more effective treatments for alcohol dependence.

Recently, neuroimaging techniques such as single photon emission computed tomography (Modell and Mountz, 1995) and functional magnetic resonance imaging (George et al., 2001) have focused on advancing the understanding of craving for alcohol. Modell and Mountz (1995) found that blood flow in the head of the right caudate nucleus increased during craving conditions, suggesting a functional role for the limbic striatum in the mediation of craving and

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impaired control over alcohol consumption. George et al. (2001) demonstrated that, after a sip of alcohol, alcoholic subjects had increased activity in the left dorsolateral prefrontal cortex and the anterior thalamus when exposed to alcohol cues, whereas social drinkers exhibited specific activation only while viewing the control beverage pictures. These authors suggested that the prefrontal cortex and anterior thalamus areas thought to be associated with emotion regulation and appetitive behavior are key brain structures for alcohol craving and addiction.

A few studies have examined electroencephalogram (EEG) responses to drug cues. Bauer and his colleagues (Bauer and Kranzler, 1994; Hersh et al., 1995) analyzed absolute EEG power to reveal no EEG abnormalities in the cocaine-dependent group under cocaine-associated film cues. In contrast, Liu et al. (1998) found that cocaine users exhibited a decrease in alpha EEG power during presentation of the drug-related stimuli compared with the neutral test session. In other words, drug cue-induced EEG changes in drug users are still unclear.

In the present study, we examined EEG changes in alcoholic subjects and social drinkers using a nonlinear measure when exposed to alcohol cues, in particular the complexity of EEG recordings. The complexity of the EEG usually is quantified by the dimensional complexity (D_2). The D_2 reflects the number of independent variables that are necessary to describe the behavior of a dynamic system. Although it has been used in some fields to differentiate between periodic, chaotic, or stochastic dynamics, the D_2 often has been used as a measure of complexity of the time series. Thus, an increase in D_2 values of the EEG suggests high activation (complexity) of cortical regions or active information processing of the cerebral cortex.

This study sought to determine (1) whether EEG changes are detected in alcoholic subjects using the D_2 when exposed to alcohol cue, and (2) if so, whether specific regions are differentially activated after viewing alcohol cues compared with neutral beverage cues, and (3) whether this change differed in magnitude or location from that in social drinkers. To answer these questions, we recruited 15 adult alcoholic subjects and 10 age- and gender-matched healthy social drinking controls. Subjects were serially rated for alcohol craving after presentations of pictures of nonalcoholic and alcohol beverages. After the picture presentation, the EEG was recorded with eyes closed, and the D_2 values were estimated and compared.

METHODS

Subjects

Fifteen alcoholic subjects (four women, mean age [standard deviation], 35 [4.5] years) who met the DSM-IV criteria (American Psychiatric Association, 1994) for current alcohol dependence were recruited. They had at least 5 years of alcohol abuse history and had completed an inpatient alcohol detoxification 2 weeks before study participation. All 15 subjects had received lorazepam (mean dose 1.13 [0.23] mg) for the treatment of alcohol withdrawal symptoms and were medication-free for at least 12 days before the EEG recoding. The following subjects were excluded from the group: subjects with mental disorders or a history of substance abuse other than alcohol, subjects whose liver enzymes were increased by 150% or more, those with a neurological disease, and females who were pregnant or breast-feeding.

Table 1. Demographic of Subjects

	Alcoholic subjects, mean (SD)	Social drinkers, mean (SD)
No.	15	10
Sex		
Female	4	3
Male	11	7
Age, years	35 (4.5)	34 (5.6)
Standard drink/day*	11.93 (1.90)	0.90 (0.46)
Drinking day, %*	65.3 (11.9)	18 (7.9)

* $p < 0.001$.

As a control group, 10 social drinking subjects (three women, age 34 [5.6] years) were recruited based on gender and age to match the alcoholic subject group (Table 1). They had no previous history of mental or neurological disorders and were alcohol-free at least 1 week before this study. A prior written informed consent was obtained from all participating subjects, and the research plan was approved by the hospital's Ethics Committee. Before participation, all subjects received physical and neurological tests as well as hematologic tests including electrolytes and complete blood cell count. Social-drinking control subjects were also medication-free for a minimum of 12 days before the study.

Experimental Procedure

Alcohol and nonalcohol beverage picture cues were drawn primarily from advertisements in several contemporary magazines and scanned on a flatbed scanner. Two 160 sec sessions for stimulus presentation were prepared on an IBM computer. Each session contained four blocks of 40 sec: resting, activation, resting, and activation. Rest blocks consisted of a blank screen. During the activation blocks, either alcohol or nonalcohol picture cues were displayed for 2 sec each. The activation blocks in the first session consisted of 20 individual nonalcohol pictures, whereas the activation blocks in the second session consisted of 20 individual alcohol pictures. EEG recordings were performed immediately after the cue presentation of each session. Nonlinear dynamic methods need long stationary EEG sequences to reconstruct the attractor in the phase space. Thus, the EEG was recorded after the cue presentation to remove electro-oculographic, movement artifacts and electrical responses to visual stimulation as much as possible. After each session, measurements for the extent of alcohol desire, alcohol craving, anxiety, and depression were made by Visual Analog Scale (VAS), similar to that used by Modell and Mountz (1995). The scale consisted of the following items: desire for an alcoholic beverage (0 = none, 10 = extreme), general level of anxiety (0 = none, 10 = extreme), prevailing mood (0 = extremely sad, 10 = extremely happy), and craving for an alcoholic beverage (0 = none, 10 = extreme). Each session was separated by 60 min to remove the effect of previous cues.

EEG Recording

EEGs were measured from each subject after each session. They were recorded from 16 scalp loci (F_7, T_3, Fp_1, F_3, C_3, P_3, O_1, F_8, T_4, T_5, T_6, Fp_2, F_4, C_4, P_4, and O_2) of the international 10–20 system. With the subjects in a relaxed state and eyes closed, 32.678 sec of continuous EEG recording (16,384 data points at a sampling frequency of 500 Hz) was acquired and digitized using a 12-bit analog-digital converter on an IBM PC. Potentials from the 16 channels referenced against linked earlobes were amplified on a San-Ei EE1121 machine using a time constant of 0.1 sec. Overall amplification was 20,000-fold. Each EEG record was judged to be free from electro-oculographic and movement artifacts and to contain minimal electromyographic activity.

Power Spectrum Analysis

The EEG was digitized, and fast Fourier transformation was performed. To calculate EEG power, the frequency spectrum was divided into 0.2 Hz bands and collapsed into EEG frequency bands of delta (0.1–3.9 Hz), theta (4.0–7.9 Hz), alpha (8.0–12.9 Hz), and beta (13.0–35.0 Hz). Each power value represented 5 sec, and we analyzed 30 sec of recording per case. Then we designated these power values as average percentages of total power (Coben et al., 1983). These were usually called delta, theta, alpha, and beta power ratios.

Nonlinear Dynamic Analysis

The dimensional complexity (D_2) reflects the number of independent variables that are essential for describing the dynamics of the concerned system. In general, the larger the value of D_2, the more complex the behavior of the system. D_2 values of EEG signals were estimated using the Grassberger-Procaccia algorithm. Although the neurophysiological meaning of the complexity is not clear, the complexity can be interpreted as the integration of information in the brain (Tononi et al., 1998). This includes both the integration of the activity of functionally segregated neuronal groups and the integration of incoming stimuli with ongoing, spontaneous brain activity.

Nonlinear analyses usually are performed in the phase space. In the *n*-dimensional phase space, each state of the system corresponds to a single point in the phase space whose *n* coordinates are the values assumed by the governing variables for this specific state. If the system is observed through time, the sequence of points in the phase space forms a dynamic trajectory. This trajectory fills a subspace of the phase space, which is called the system's attractor.

However, in most biological systems, we are unable to obtain the actual underlying equations that generate complex behaviors but only to observe temporal sequences of events
. Thus, the attractor is reconstructed in the phase space from the observed sequences
by plotting delay coordinates in what is referred to as an embedding procedure (Eckmann and Ruelle, 1985). The delay coordinates $y(t) = [x(t), x(t + T),\ldots, x(t + (d - 1)T)]$ are constructed from an observed single time series x(t), where T is the time delay and *d* is the embedding dimension, to unfold the projection back to a multivariate phase space that is a representation of the original system. An attractor reconstructed in an embedding procedure by using delay coordinates from a single time series x(t) is topologically equivalent to the original dynamic system (Takens, 1981).

For the time delay T, the first local minimum of the average mutual information between the set of measurement x(t) and x(t + T) often is used. Mutual information measures linear and nonlinear dependence of two variables (Fraser and Swinney, 1986).

Using the Grassberger-Procaccia algorithm, we evaluated the D_2 of the attractors from the delay coordinates obtained by the EEG sequences (Grassberger and Procaccia, 1983). In this algorithm, the D_2 calculation is based on determining the relative number of pairs of points in the phase-space data set that are separated by a distance less than r. It is computed from

$$D_2 = \lim_{r\to 0}\lim_{N\to\infty}\frac{\log C(r,N)}{\log r}, \qquad (1)$$

where the correlation integral $C(N, r)$ is defined by

$$C(r,N) = \frac{2}{(N-W)(N-1-W)}\sum_{i=1}^{N}\sum_{j=i+1+W}^{N}\theta(r - |\vec{x}_i - \vec{x}_j|), \qquad (2)$$

where x_i and x_j are the points of the trajectory in the phase space, *N* is the number of data points in the phase space, the distance *r* is a radius around each reference point x_i, and θ is the Heaviside function, defined as 0 if $x < 0$, and 1 if $x \geq 0$. W denotes the Theiler correction (Theiler, 1986), which was used to correct for temporal correlations. A short plateau can be detected in the D_2 curve of EEG sequences for an appropriate combination of small values of delay time and Theiler correction W.

For small *r*, a scaling property is exhibited: $C(N, r) \propto r^{D2}$. For a self-similar (fractal) attractor the local scaling exponent is constant, and this is called a scaling region. If this plateau is present over a significant long range, the scaling exponent can be used as an estimate of the D_2. $C(N, r)$ is plotted against *r* on a log-log scale, and the D_2 is given by the slope of this curve over a selected range of *r*. In this study, the slope of the correlation integral curve in the scaling region was estimated by a linear regression method. We used a modification, proposed by Kantz and Schreiber (1997), of the Grassberger-Procaccia algorithm to removes pairs of points that are temporally close from consideration. More detailed algorithm and meaning of the D_2 are found in reviews (Abarbanel and Rabinovich, 2001; Faure and Korn, 2001; Jeong, 2002).

The surrogate data test was used to confirm the presence of the nonlinear structure in the EEG signals. Surrogate data are a randomized sequence of the original data with all nonlinear determinism that may be present destroyed (Schreiber and Schmitz, 2000). Thus, a statistically significant difference in the D_2 values between original data and the surrogate data would indicate the presence of nonlinear determinism in the original data. In our analysis, the D_2 estimation was applied to each raw EEG data set and 20 different sets of surrogates. Pairwise *t* tests of the difference between the D_2 values of the original EEG data and the mean D_2 values of their 20 surrogates were applied to test the null hypothesis of a linear stochastic behavior.

Statistical Analysis

With respect to D_2 values and craving-related VAS, the changes that occurred after the presentation of neutral and alcohol cues were analyzed using group by condition by electrode site or scales of repeated-measures ANOVA (SPSS 9.0 for Windows). Pearson correlation coefficients were used to examine the relationship of the changing subscale of VAS (alcohol craving, desire to drink) and changes in D_2 values with alcoholic patients. We considered $p < 0.05$ to be significant. All data were expressed as mean [standard deviation].

RESULTS

After cue presentations, the VAS was estimated for each subject to quantify a desire to drink, anxiety, depression, and alcohol craving. The alcoholic subjects exhibited a significantly high desire to drink (3.4 [1.72]) and a higher alcohol craving (3.87 [1.8]) compared with those (0.2 [0.42] for a desire to drink, 0.8 [0.68] for alcohol craving) of the control subjects [desire to drink: $F(1,23) = 37.559$, $p < 0.001$; alcohol craving: $F(1,23) = 42.741$, $p < 0.001$, interaction effects]. No significant differences in the category of anxiety and depression were found between the two groups [anxiety: $F(1,23) = 0.137$, $p = 0.715$; depression: $F(1,23) = 1.288$, $p = 0.288$, Table 2]. The cue presentation of main effect indicated that a desire to drink, alcohol craving, and anxiety were greater during alcohol cue exposure in all subjects [desire to drink: $F(1,23) = 42.918$, $p < 0.001$; alcohol craving: $F(1,23) = 55.501$, $p < 0.001$; anxiety: $F(1,23) = 11.067$, $p = 0.003$].

A comparison of EEG power values between the alcoholic subjects and social drinking controls showed no significant differences in all channels after viewing alcohol cues compared with viewing beverage cues (Table 3). However, a tendency to exhibit a decrease in alpha power in the

Table 2. Summary for VAS for Alcoholic Subjects and Social Drinking Controls

Assessment item	Alcoholic subjects (n = 15)	Social drinking controls (n = 10)	p
Desire for alcohol			
Neutral stimulus	0.40 (0.63)	0.10 (0.32)	0.000*
Alcohol stimulus	3.40 (1.72)	0.20 (0.42)	
Anxiety			
Neutral stimulus	0.67 (0.72)	0.50 (0.53)	
Alcohol stimulus	1.07 (0.70)	1.00 (0.82)	0.715
Mood			
Neutral stimulus	5.60 (0.74)	4.90 (0.74)	
Alcohol stimulus	5.53 (0.92)	5.30 (0.48)	0.288
Craving for alcohol			
Neutral stimulus	0.80 (0.68)	0 (0)	
Alcohol stimulus	3.87 (1.80)	0.80 (0.68)	0.000*

Values are mean (SD).

* $p < 0.05$ with respect to differences between groups by repeated measures ANOVA.

right inferior frontal (F_8) in alcoholic patients was detected [$F(1,23) = 4.276$, $p = 0.05$].

Nonlinear analysis of the EEG recorded from each subject after each session using the surrogate data method found significant differences of D_2 values of about 0.8 to 1.2 between raw EEG data and their surrogate data in all channels ($p < 0.001$). This result confirms the presence of a nonlinear structure within the EEG and therefore the validity of the application of nonlinear dynamic methods to the EEG used in this study.

A comparison of the D_2 values of each EEG epoch between the alcoholic subjects and social drinking controls (interaction effects) revealed a significant increase in the D_2 values of the EEG in the frontal (F_3, F_4), right posterior temporal (T_6), and occipital (O_1, O_2) regions after viewing alcohol cues compared with viewing beverage cues in alcoholic subjects (F_3). This result indicates that more complex (or higher) cortical activity is induced over specific brain regions of the alcoholic subjects after alcohol cue exposure. The cue presentations of main effect indicated that D_2 value was greater during alcohol cue exposure at the left anterior temporal (T_3), left parietal (P_3), left frontal (F_4), and right parietal (P_4) regions [T_3: $F(1,23) = 7.815$, $p = 0.010$; P_3: $F(1,23) = 9.533$, $p = 0.005$; F_4: $F(1,23) = 4.822$, $p = 0.038$; P_4: $F(1,23) = 7.409$, $p = 0.012$].

Changes in subscale of alcohol craving between the nonalcohol and alcohol picture were found to be significantly correlated with changes in D_2 values in the left frontal (F_3) region in alcoholic subjects ($p = 0.030$). The right posterior temporal region (T_6) showed a tendency to exhibit a correlation between subscale and D_2 values ($p = 0.06$). In addition, changes in the subscale "a desire to drink" between the nonalcohol and alcohol picture were not significantly correlated with changes in D_2 values in the left frontal (F_3) region in alcoholic subjects ($p = 0.057$).

DISCUSSION

To our knowledge, this is the first report using nonlinear methods to examine the EEG responses induced by visual cues with alcohol. We demonstrate that alcoholic subjects, compared with social drinking controls, report higher rates of craving at baseline while viewing alcohol-related cues. Alcoholic subjects had significantly higher complexity of the EEG than social drinking controls after exposure to alcohol-specific visual cues. Furthermore, the specific regions activated in alcoholic subjects after alcohol cue exposure were found to be the frontal, right posterior temporal, and occipital regions. By contrast, social drinking controls did not show any significant changes in complexity of the EEG between alcohol and nonalcohol cue sessions. In addition, changes in the subscale of alcohol craving between alcohol and nonalcohol cue sessions were correlated with D_2 changes in the left frontal region in alcoholic subjects. However, no significant change in EEG power was detected in alcoholic and social drinking subjects after viewing alcohol cues compared with viewing beverage cues. These findings indicate that alcohol craving results in the more complex EEG behavior in the frontal, right posterior temporal, and occipital regions. We suggest that nonlinear measures like the D_2 are useful tools for quantifying these EEG responses, which cannot be detected by conventional linear analysis, and for investigating the neural aspects of alcohol craving and relapse to alcohol use.

The specific regions of changes in the EEG complexity after alcohol cue exposure are frontal, right posterior temporal, and occipital regions. Given that the EEG complexity reflects the integration of the activity of functionally separated neuronal populations or the integration of incoming stimuli with ongoing brain activity, the increased complexity indicates more activation in these regions in alcoholic subjects during alcohol-specific cue presentation. Despite the different experimental paradigms, the specific regions found in the current study are likely in accordance with previous imaging studies on alcoholics during alcohol cue stimulation. George et al. (2001) found the prefrontal cortex and the anterior paralimbic cortex to be the activation regions during alcohol-specific cue exposure. Studies on craving for cocaine or substances other than alcohol also reported that the frontal region is a key brain structure for craving (Grant et al., 1996; Maas et al., 1998; Volkow et al., 1999). In addition, the basal ganglia and limbic striatal and thalamocortical regions also are involved in craving and loss of control in alcohol dependence (Modell and Mountz, 1995; Modell et al, 1990). Wang et al. (1999), using positron emission tomography, found that cocaine craving is associated with the activation of the right insula. Although the EEG recording has a low spatial resolution, the findings in this study support that frontal and temporal regions are activated during alcohol-specific cue presentations. These specific regions are thought to be associated with emotion regulation, attention, and appetitive behavior (George et al., 2001).

In the present study, a few limitations warrant further discussion. First, we had a relatively small sample size of alcoholic and control subjects. To draw more reliable con-

Table 3. Alpha, Beta, Theta, and Delta Activities of the EEG for Alcoholic Subjects and Healthy Controls After Neutral and Alcohol-Specific Cue Presentations

Channel		Alcoholic subjects (n = 15)		Social drinking controls (n = 10)			
		Neutral cue	Alcohol-specific cue	Neutral cue	Alcohol-specific cue	F	p
F3	Alpha	0.399 (0.213)	0.388 (0.28)	0.531 (0.199)	0.604 (0.076)	0.711	0.408
	Beta	0.249 (0.255)	0.411 (0.303)	0.083 (0.089)	0.148 (0.080)	1.180	0.289
	Theta	0.242 (0.191)	0.109 (0.099)	0.175 (0.132)	0.124 (0.139)	1.313	0.264
	Delta	0.109 (0.080)	0.091 (0.041)	0.210 (0.110)	0.122 (0.087)	1.715	0.203
F4	Alpha	0.442 (0.181)	0.370 (0.288)	0.553 (0.202)	0.615 (0.103)	2.420	0.100
	Beta	0.254 (0.203)	0.351 (0.311)	0.083 (0.057)	0.090 (0.073)	1.270	0.271
	Theta	0.188 (0.109)	0.118 (0.092)	0.017 (0.129)	0.121 (0.085)	0.207	0.653
	Delta	0.115 (0.079)	0.160 (0.118)	0.193 (0.172)	0.172 (0.140)	0.899	0.353
F7	Alpha	0.338 (0.242)	0.239 (0.260)	0.075 (0.154)	0.014 (0.069)	0.078	0.782
	Beta	0.235 (0.231)	0.128 (0.189)	0.215 (0.073)	0.134 (0.083)	0.129	0.722
	Theta	0.258 (0.122)	0.404 (0.226)	0.484 (0.212)	0.495 (0.243)	1.851	0.187
	Delta	0.168 (0.162)	0.201 (0.221)	0.224 (0.213)	0.356 (0.258)	3.298	0.082
F8	Alpha	0.302 (0.245)	0.153 (0.099)	0.304 (0.270)	0.323 (0.189)	4.276	0.050
	Beta	0.305 (0.280)	0.251 (0.254)	0.052 (0.074)	0.029 (0.018)	0.153	0.699
	Theta	0.254 (0.125)	0.382 (0.253)	0.452 (0.230)	0.478 (0.250)	0.925	0.346
	Delta	0.137 (0.145)	0.213 (0.264)	0.191 (0.067)	0.170 (0.103)	2.160	0.155
Fp1	Alpha	0.403 (0.291)	0.394 (0.211)	0.204 (0.139)	0.164 (0.144)	0.114	0.739
	Beta	0.226 (0.199)	0.171 (0.074)	0.284 (0.217)	0.280 (0.228)	0.275	0.605
	Theta	0.221 (0.206)	0.310 (0.204)	0.280 (0.242)	0.394 (0.275)	0.052	0.821
	Delta	0.149 (0.140)	0.121 (0.084)	0.231 (0.125)	0.161 (0.075)	0.675	0.420
Fp2	Alpha	0.473 (0.248)	0.408 (0.201)	0.323 (0.101)	0.196 (0.154)	1.148	0.295
	Beta	0.239 (0.218)	0.316 (0.173)	0.327 (0.215)	0.392 (0.231)	1.485	0.235
	Theta	0.158 (0.157)	0.191 (0.099)	0.146 (0.212)	0.295 (0.241)	0.038	0.846
	Delta	0.130 (0.124)	0.079 (0.049)	0.175 (0.089)	0.116 (0.077)	0.031	0.861
T3	Alpha	0.628 (0.234)	0.487 (0.244)	0.290 (0.173)	0.301 (0.216)	3.007	0.096
	Beta	0.222 (0.203)	0.168 (0.199)	0.230 (0.114)	0.164 (0.062)	2.466	0.130
	Theta	0.160 (0.129)	0.190 (0.180)	0.207 (0.102)	0.211 (0.378)	0.072	0.791
	Delta	0.040 (0.044)	0.157 (0.178)	0.192 (0.172)	0.259 (0.173)	0.351	0.560
T4	Alpha	0.636 (0.186)	0.568 (0.220)	0.330 (0.214)	0.408 (0.220)	1.061	0.314
	Beta	0.176 (0.165)	0.177 (0.116)	0.210 (0.097)	0.170 (0.225)	0.011	0.917
	Theta	0.124 (0.076)	0.127 (0.101)	0.283 (0.169)	0.290 (0.242)	0.002	0.962
	Delta	0.061 (0.080)	0.125 (0.133)	0.172 (0.144)	0.127 (0.121)	0.651	0.428
T5	Alpha	0.359 (0.215)	0.402 (0.210)	0.300 (0.331)	0.480 (0.385)	0.015	0.903
	Beta	0.364 (0.221)	0.251 (0.253)	0.413 (0.294)	0.182 (0.158)	1.251	0.275
	Theta	0.120 (0.078)	0.180 (0.196)	0.138 (0.126)	0.078 (0.070)	2.580	0.122
	Delta	0.095 (0.101)	0.142 (0.118)	0.138 (0.101)	0.199 (0.272)	0.029	0.867
T6	Alpha	0.379 (0.162)	0.461 (0.234)	0.420 (0.263)	0.434 (0.311)	1.008	0.326
	Beta	0.343 (0.238)	0.270 (0.248)	0.195 (0.179)	0.155 (0.230)	0.024	0.877
	Theta	0.168 (0.170)	0.140 (0.047)	0.208 (0.158)	0.171 (0.238)	0.009	0.927
	Delta	0.108 (0.078)	0.122 (0.090)	0.176 (0.187)	0.239 (0.752)	1.985	0.172
C3	Alpha	0.368 (0.296)	0.406 (0.308)	0.277 (0.312)	0.406 (0.308)	0.120	0.732
	Beta	0.274 (0.299)	0.303 (0.251)	0.298 (0.266)	0.231 (0.292)	1.207	0.283
	Theta	0.162 (0.206)	0.134 (0.137)	0.074 (0.297)	0.156 (0.013)	0.935	0.344
	Delta	0.090 (0.117)	0.156 (0.163)	0.280 (0.172)	0.135 (0.201)	0.232	0.635
C4	Alpha	0.408 (0.292)	0.400 (0.286)	0.326 (0.223)	0.206 (0.175)	3.407	0.078
	Beta	0.259 (0.264)	0.310 (0.260)	0.335 (0.282)	0.328 (0.251)	1.760	0.198
	Theta	0.081 (0.057)	0.125 (0.120)	0.224 (0.261)	0.296 (0.166)	0.185	0.671
	Delta	0.200 (0.145)	0.153 (0.120)	0.113 (0.0531)	0.158 (0.0333)	2.533	0.126
P3	Alpha	0.354 (0.275)	0.445 (0.336)	0.104 (0.081)	0.149 (0.133)	0.173	0.681
	Beta	0.230 (0.184)	0.203 (0.271)	0.403 (0.212)	0.304 (0.261)	0.105	0.749
	Theta	0.246 (0.167)	0.195 (0.200)	0.266 (0.0945)	0.290 (0.297)	0.858	0.364
	Delta	0.170 (0.167)	0.155 (0.194)	0.226 (0.185)	0.214 (0.165)	0.004	0.953
P4	Alpha	0.458 (0.330)	0.488 (0.328)	0.092 (0.051)	0.144 (0.152)	0.097	0.758
	Beta	0.216 (0.227)	0.233 (0.237)	0.428 (0.277)	0.335 (0.201)	3.016	0.096
	Theta	0.160 (0.191)	0.107 (0.122)	0.223 (0.191)	0.208 (0.141)	0.476	0.497
	Delta	0.166 (0.212)	0.171 (0.180)	0.257 (0.200)	0.312 (0.278)	1.143	0.296
O1	Alpha	0.226 (0.262)	0.267 (0.262)	0.418 (0.196)	0.301 (0.249)	2.409	0.134
	Beta	0.303 (0.295)	0.236 (0.225)	0.093 (0.0379)	0.080 (0.010)	0.485	0.493
	Theta	0.210 (0.215)	0.207 (0.236)	0.132 (0.136)	0.225 (0.282)	0.068	0.417
	Delta	0.119 (0.117)	0.284 (0.205)	0.257 (0.214)	0.347 (0.278)	3.765	0.065
O2	Alpha	0.256 (0.127)	0.185 (0.165)	0.352 (0.179)	0.294 (0.178)	0.028	0.869
	Beta	0.312 (0.319)	0.439 (0.377)	0.153 (0.123)	0.140 (0.161)	2.000	0.171
	Theta	0.261 (0.226)	0.119 (0.120)	0.313 (0.203)	0.351 (0.290)	2.037	0.167
	Delta	0.169 (0.163)	0.256 (0.278)	0.181 (0.126)	0.214 (0.301)	0.224	0.64

* $p < 0.05$ in difference between groups by repeated measures ANOVA.

Table 4. Average D_2 Values of the EEG for Alcoholic Subjects and Healthy Controls After Neutral and Alcohol-Specific Cue Presentations

	Alcoholic subjects (n = 15)		Social drinking controls (n = 10)		
Channel	Neutral cue	Alcohol-specific cue	Neutral cue	Alcohol-specific cue	p
F_3	7.790 (0.744)	8.105 (0.530)	8.313 (0.278)	7.982 (0.450)	0.012*
F_4	7.432 (2.010)	7.857 (0.425)	8.259 (0.195)	5.955 (2.147)	0.004*
F_7	7.721 (0.742)	7.324 (2.204)	8.593 (0.433)	7.544 (1.056)	0.269
F_8	7.427 (1.821)	7.459 (1.866)	7.700 (0.610)	8.060 (0.384)	0.683
Fp_1	7.624 (0.763)	6.673 (2.519)	8.378 (0.455)	8.290 (0.168)	0.271
Fp_2	7.579 (0.777)	7.057 (1.945)	7.196 (1.362)	7.880 (0.266)	0.118
T_3	8,003 (0.539)	8.302 (0.469)	6.851 (2.900)	8.286 (0.547)	0.080
T_4	8.121 (0.480)	8.124 (0.275)	7.881 (0.369)	7.874 (0.427)	0.958
T_5	8.128 (0.581)	7.646 (1.878)	7.803 (1.151)	8.104 (0.740)	0.169
T_6	7.849 (0.398)	7.942 (0.462)	7.982 (0.330)	7.071 (0.263)	0.000*
C_3	8.258 (0.360)	8.180 (0.726)	7.792 (0.357)	8.129 (0.632)	0.138
C_4	8.128 (0.779)	7.800 (0.606)	7.300 (0.305)	7.345 (0.497)	0.505
P_3	7.895 (0.441)	7.980 (0.403)	7.838 (0.555)	8.134 (0.464)	0.101
P_4	7.781 (0.622)	7.202 (2.119)	7.556 (0.438)	5.367 (2.622)	0.127
O_1	7.357 (0.827)	7.835 (0.412)	7.994 (0.450)	7.836 (0.659)	0.004*
O_2	7.431 (0.588)	7.921 (0.640)	7.902 (0.332)	7.047 (0.956)	0.001*

* $p < 0.05$ in difference between groups by repeated measures ANOVA.

Table 5. Correlation Coefficient and p Value Betweeen Changes of Scale for Alcohol (Craving and Desire) and Dimensional Complexity for the Patients With Alcohol Dependence

	Craving for alcohol		Desire for alcohol	
Location	Pearson correlation coefficient	Significance (p value)	Pearson correlation coefficient	Significance (p value)
F_3	0.560	0.030*	0.501	0.057
F_4	0.338	0.217	0.338	0.218
F_7	0.121	0.667	0.105	0.708
F_8	0.094	0.739	0.075	0.790
Fp_1	−0.011	0.970	0.073	0.797
Fp_2	0.037	0.896	0.131	0.641
T_3	0.386	0.156	−0.254	0.361
T_4	−0.99	0.724	−0.012	0.965
T_5	−0.362	0.185	−0.241	0.387
T_6	0.497	0.060	0.399	0.140
C_3	0.215	0.442	0.230	0.409
C_4	0.113	0.689	0.052	0.854
P_3	0.138	0.623	0.191	0.496
P_4	0.101	0.721	0.097	0.730
O_1	0.041	0.100	0.400	0.139
O_2	0.166	0.553	0.131	0.642

* $p < 0.05$.

clusions, this study needs replication with larger samples. In addition, to assess neural correlates of alcohol craving, we should measure subjective craving in real time during the EEG recording and cue presentation and plan to perform analyses directly investigating changes in electrocortical activity that temporally correlate with subjective craving for alcohol (George et al., 2001). Finally, the visual control pictures used in this study did not match the alcohol cues in color and hue. This discrepancy might produce differences in the EEG complexity in occipital regions of alcoholic subjects between alcohol and nonalcohol cue presentation, although healthy controls did not exhibit any EEG changes in the occipital region between two presentations. Thus, it is possible that the occipital region is not directly associated with alcohol craving.

CONCLUSION

This study suggests that changes in electrical brain activity followed by viewing alcohol cues can be evaluated by an EEG recording and nonlinear methods. When exposed to alcohol cues, alcoholic subjects had increased complexity in cortical activity in the frontal, right posterior temporal, and occipital regions. These areas can be target brain regions for future studies on alcohol craving and addiction. In addition, this study proposes that nonlinear analysis of the EEG can be a useful tool to assess alcohol cue-induced brain activity in alcohol dependence at a relatively small cost. In addition, this study proposes that nonlinear analysis of the EEG can be a useful tool to assess alcohol cue-induced brain activity in alcohol dependence at a relatively small cost.

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