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5 **ON THE COMPLEXITY AND ENERGY ANALYSES**  
 6 **IN EEG BETWEEN ALCOHOLIC AND CONTROL**  
 7 **SUBJECTS DURING DELAYED MATCHING**  
 8 **TO SAMPLE PARADIGM**

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15 Received  
 16 Revised

17 In this study, we have investigated the electrophysiological differences between alco-  
 18 holic and control subjects using two different approaches namely complexity and energy  
 19 (power) analyses. The electroencephalogram data used in this study were recorded from  
 20 77 alcoholic and 44 control subjects while the subjects were performing delayed matching  
 21 to sample object recognition task for three types of stimuli. These were a single stimulus  
 22 and a second matching or nonmatching stimulus that followed the single stimulus after  
 23 a delay. The experimental paradigm evokes object recognition, visual short-term mem-  
 24 ory, and decision-making abilities. The results indicated that all regions (i.e. frontal,  
 25 central, temporal, parietal, and occipital) in the brain exhibit more complexity and less  
 26 energy for alcoholic subjects as compared to controls. When different visual stimuli pairs  
 27 were compared among alcoholic and control subjects, the results from energy analysis  
 28 showed groupwise differences in occipital and parietal regions. These results provide a  
 29 strong indication on the impairment in brain's electrophysiological activity for alcoholic  
 subjects due to a history of long-term alcohol abuse.

*Keywords:* Alcohol abuse; electroencephalogram; energy analysis; nonlinear complexity.

31 **1. Introduction**

32 Addiction based diseases are the major cause of concern in the society. Among these  
 33 addiction based diseases, alcohol related health disorders are the most frequent. It  
 34 is known that even moderate alcohol consumption leads to short-term memory  
 35 impairments and blackouts. These impairments could cause accidents in some jobs  
 36 such as drivers, pilots, and machinery operators since it is critical to make fast  
 37 and correct decisions. Therefore, it is important to investigate whether long-term  
 alcohol abuse has permanent effect on memory, attention, and decision making.

38 In recent years, considerable research has been done to investigate the effects  
 39 of long-term alcohol abuse on the brain. Literature reviews have shown that heavy

2 *T. Balli & R. Palaniappan*

1 drinking may have large scale effects ranging from short-term memory loss to black-  
outs in some of the alcoholics.<sup>1</sup>

3 Electroencephalogram (EEG) is a representative signal that contains useful  
4 information about the electrical activity of the brain. Due to its noninvasive nature,  
5 the analysis of EEG signals has become increasingly attractive in recent years (i.e.  
6 for neurophysiological studies and clinical purposes). One of the most important  
7 applications using EEG is analysis of brain electrical activity under various con-  
8 ditions such as sleep disorders, epilepsy, mania, and depression.<sup>2</sup> In this paper,  
9 we have utilized Visual Evoked Potential (VEP) signals, which is a type of Event  
10 Related Potential (ERP) that is evoked by external visual stimulus, for investigat-  
11 ing the electrophysiological differences between alcoholic and control (nonalcoholic)  
12 subjects during delayed matching to sample paradigm. Note that ERP is the evoked  
13 component in the EEG signals in response to an external stimulus such as visual,  
14 auditory or somatosensory.

15 Previous research studies using EEG and VEP signals have shown that the  
16 brain activity of alcoholic and control subjects differs in numerous aspects.<sup>1,3-9</sup>  
17 In particular, when considering the difference in event related potentials between  
18 alcoholics and nonalcoholics, these researchers focused on several ERP components  
19 such as c240 and c320,<sup>1</sup> P300,<sup>4-7,10</sup> N400,<sup>4,5</sup> contingent negative variation (CNV),  
20 and mismatch negativity (MMN).<sup>5</sup> However, there has been no reported study that  
21 compared complexity or energy of brain signals of alcoholics evoked during delayed  
22 matching to sample paradigm.

23 In this study, we set out to analyze the complexity and energy of VEP signals  
24 obtained from alcoholic and control subjects. In the study by Natarajan *et al.*,<sup>11</sup>  
25 it was suggested that using nonlinear measures would be a better approach for  
26 the complexity analysis of brain signals since these signals exhibit irregular behav-  
27 ior with nonlinear dynamical properties. As such, we have utilized Approximate  
28 Entropy (ApEn), which is a commonly used nonlinear measure of complexity. Using  
29 complexity and energy analysis approaches, we set out to show that there are sig-  
nificant electrophysiological differences between alcoholics and controls.

## 31 **2. Methodology**

### 32 **2.1. Subjects**

33 The EEG signals used in this study were recorded from 121 male subjects where  
34 77 of the subjects were alcoholics and the rest were control subjects. The mean age  
35 of the alcoholic group was 35.83 years with SD = 5.33 ranging from 22.33 to 49.8  
36 years old while the mean age of control group was 25.81 years old with SD = 3.38  
37 ranging from 19.4 to 38.6 years old. The alcoholic subjects were significantly older  
38 than the control subjects [ $t(118.9) = 12.64, p = 0.0001$ ].

39 In the paper by Rourke *et al.*,<sup>9</sup> the effects of age and length of abstinence on the  
recovery of neuropsychological functioning in male alcoholics have been discussed.

1 According to their results, both recently detoxified and alcoholics that have been  
2 sober for 2 years and who were older than 50 years of age performed worse on visual  
3 recall compared to similarly aged long-term abstinent alcoholics and nonalcoholic  
4 subjects, on the other hand all the participants less than 50 years of age performed  
5 at comparable levels. In this study, all of the subjects were younger than 50 years  
6 old so we did not employ analyses of covariance controlling for age.

7 Most of the alcoholic subjects had been drinking heavily for 15 years, starting  
8 approximately at the age of 20. The diagnosis of alcohol dependence was made  
9 by the intake of the addictive disease hospital in Brooklyn according to DSM-III  
10 criteria. The alcoholic subjects had not been drinking and taking any medication  
11 for a minimum of one month, therefore all of them were fully detoxified during that  
12 period of time. The alcoholic subjects that had a history of overt liver, metabolic,  
13 vascular, and neurological diseases, major psychiatric illness or drug dependence  
14 were excluded from the study.

15 The control subjects had no personal or family histories of alcohol or drug  
16 dependence and the ones having any history of neurological or major psychiatric  
17 illness were excluded from the study.

All subjects had normal vision or corrected normal vision.

## 19 **2.2. Mental task**

20 In this study, the subjects were exposed to two consecutive visual stimuli. The  
21 visual stimuli were pictures of objects selected from Snodgrass and Vanderwart  
22 picture set.<sup>12</sup> These pictures were common black and white line pictures which can  
23 be recognized easily by all subjects such as banana, kite, aeroplane, ball, bicycle,  
24 etc. These simple pictures were used to avoid possible ambiguity since some amnesic  
25 subjects cannot recognize complex pictures easily.<sup>13</sup> Figure 1 shows some examples  
26 of Snodgrass and Vanderwart pictures.

27 In order to preserve the consistency of the representation of the pictures, the  
pictures were grouped into different categories according to their semantic category

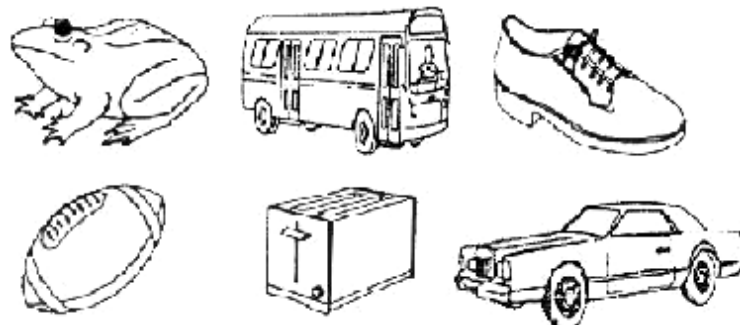


Fig. 1. Some examples from Snodgrass and Vanderwart picture set.

4 *T. Balli & R. Palaniappan*

1 within the brain such as four footed animal, fruit, weapon, musical instrument, etc.  
 2 The pictures were presented such that if the first visual stimulus is from one group,  
 3 the second visual stimulus will be from another group.

### 2.3. *Subjects' task*

5 The task assigned to the subjects was to decide whether the first and the second  
 6 pictures presented to them were matching or nonmatching. The subjects were asked  
 7 to press a mouse key in one hand if the pictures were same and press a mouse key  
 8 in the other hand if the pictures were different. The selection of the hand indicating  
 9 the matching and nonmatching was altered between subjects.

### 2.4. *Recording*

11 The subjects were seated in a reclining chair located in a sound proof, RF shielded  
 12 room during the recording session. The EEG signals were recorded for one sec-  
 13 ond from 64 electrodes placed on the scalp of the subject and were sampled at  
 14 256 Hz. Therefore, a total of 256 data points were stored for each EEG signal from  
 15 every channel (electrode). The electrode placement system used was an extension

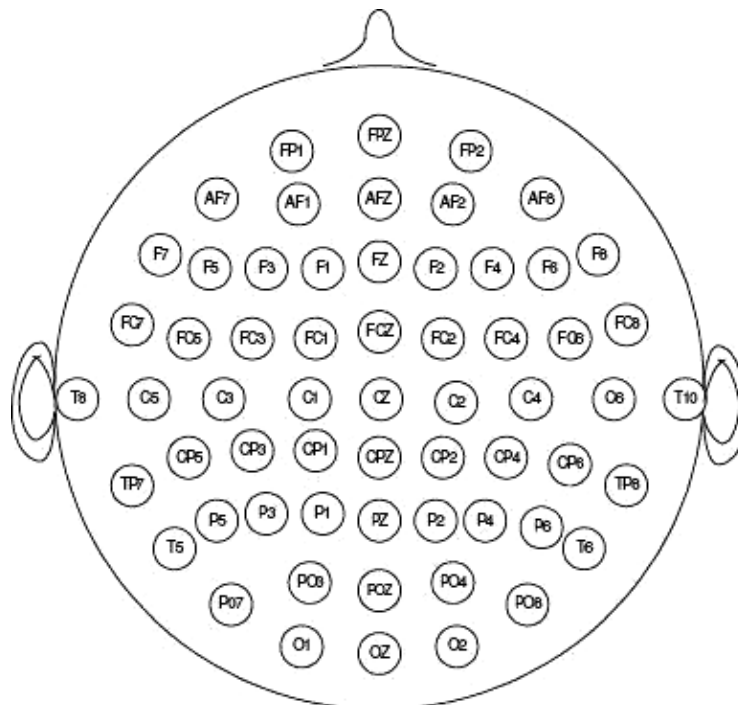


Fig. 2. 61 Channel electrode system.

1 of the 10–20 international electrode positioning system.<sup>14</sup> International 10–20 sys-  
 3 tem contains 19 active channels and two reference channels whereas the extension  
 has 61 active channels plus three reference channels. The positions of the active 61  
 channels are as shown in Fig. 2.

5 For performing regional comparison between the two groups of subjects (i.e.  
 7 alcoholics and controls), the channels were used to create vector sets belonging to  
 each region. The channels are organized such that the frontal region consisted of  
 9 Fp1, Fpz, Fp2, Af7, Af8, Af1, Af2, Afz, F7, F8, F5, F6, F3, F4, F1, F2, and Fz.  
 11 The central region consisted of Fc1, Fc2, Fc3, Fc4, Fc5, Fc6, Fc7, Fc8, Fcz, C1, C2,  
 Cp3, Cp4, Cp5, Cp6, Cpz, P1, P2, P3, P4, P5, P6, and Pz. The occipital region consisted of Po1,  
 13 Po2, Po7, Po8, Poz, O1, O2, and Oz. The temporal region consisted of T8, T10,  
 Tp7, Tp8, P7, and P8. These selections of channels were obtained from a previous  
 study.<sup>1</sup>

15 The recording of EEG was done when the subjects were performing object  
 17 recognition task as explained in the previous section. The subjects were exposed to  
 the first visual stimuli (S1) for 300 ms. After an interval of 1.6 s, the subjects were  
 19 exposed to a second visual stimulus for another 300ms which could be either in  
 matching (S2M) or nonmatching (S2N) condition. The duration between each trial  
 21 was 3.2s. This paradigm is known as the delayed matching to sample paradigm.<sup>3</sup>  
 Figure 3 shows an example of the visual stimulus presentation for the case of S2N.

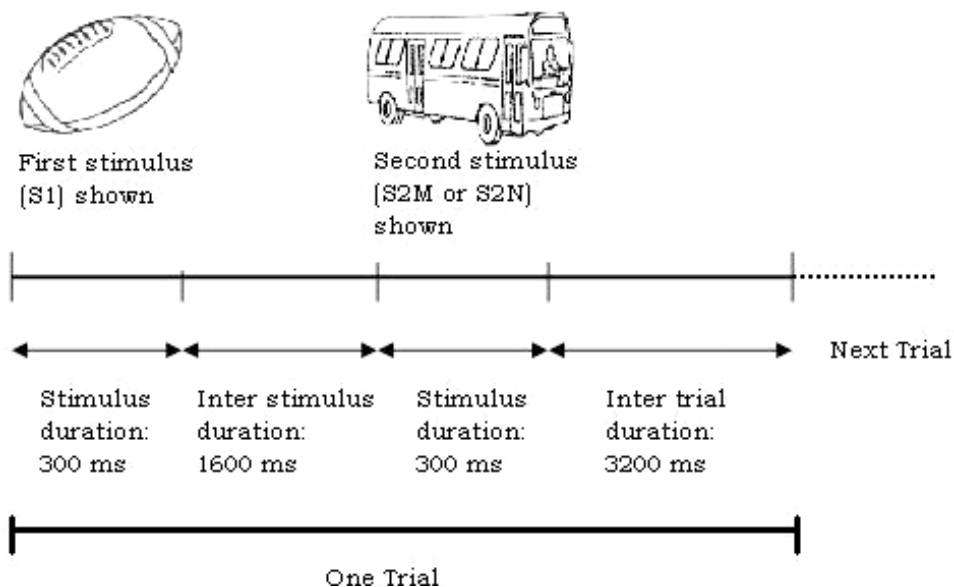


Fig. 3. An example of visual stimulus presentation in the case of S2N.

## 1 **2.5. Subjects' performances on tasks**

3 Both groups of subjects had a low response error rate for performing the task. There  
 4 were no significant differences in response errors in matching and nonmatching  
 5 trials within the groups but alcoholic subjects made more errors in matching and  
 nonmatching trials than control subjects as shown in Table 1.

7 Furthermore the stimulus condition had a significant effect on response times  
 8 of subjects where the response time to matching stimulus was significantly shorter  
 9 than nonmatching stimulus in both of the groups. Besides, in both of the stimulus  
 conditions the alcoholic subjects had a longer response time than controls as shown  
 in Table 2.

## 11 **2.6. Pre-processing**

13 In the pre-processing stage, EEG signals were first hardware (analogue) band-pass  
 14 filtered between 0.002 and 50 Hz, this is a common place to practice in practical  
 15 EEG data manipulation. After that, the EEG signals were decimated by a factor of  
 two to reduce the effective sampling frequency to 128 Hz. Aliasing effects will not  
 be a problem as the EEG signals were low pass filtered to 50 Hz earlier.

17 In the next step, eye-blink artifact contaminated EEG signals were detected and  
 18 removed from the records based on amplitude discrimination. This was achieved  
 19 using a computer program written to detect EEG signals in frontal and prefrontal  
 regions with magnitudes above  $100\ \mu\text{V}$ . The value of  $100\ \mu\text{V}$  was selected since  
 21 blinking produces a potential of  $100\text{--}200\ \mu\text{V}$  lasting for 250 ms.<sup>19</sup>

23 After removing the eye-blink contaminated signals, VEP component (which is  
 24 related to the stimulus) was extracted from the EEG signal. Basically the VEP  
 component is hidden in EEG signals and the amplitude of EEG that is not related  
 25 to the stimulus is much higher than the VEP component. Since we are interested in  
 VEP only, ensemble averaging was performed to and obtain VEP component hidden  
 27 in the EEG signals. We had a total of 5,497 EEG signals for first visual stimulus,

Table 1. The response errors during performance of mental tasks.

	Matching Stimulus (Mean $\pm$ SD)	Nonmatching Stimulus (Mean $\pm$ SD)
Alcoholic subjects	$0.62 \pm 1.11$	$0.39 \pm 0.78$
Control subjects	$0.29 \pm 0.59$	$0.12 \pm 0.31$

Table 2. The response times(ms) during performance of mental tasks.

	Matching Stimulus (Mean $\pm$ SD)	Nonmatching Stimulus (Mean $\pm$ SD)
Alcoholic subjects	$608.6 \pm 90.32$	$678.6 \pm 90.10$
Control subjects	$575.7 \pm 109.8$	$644.1 \pm 107.1$

1 2,777 EEG signals for the second matching visual stimulus and 2,720 EEG signals  
3 for second nonmatching visual stimulus belonging to 77 alcoholic and 44 control  
5 subjects. The number of trials was not the same for each subject where there was a  
7 minimum of 10 and a maximum of 50 trials from each subject. As mentioned before  
9 the VEP signals are extracted by averaging the multi-trial EEG signals from each  
subject. Upon the completion of this step, we had a total of 64 channels of VEP for  
each S1, S2M, and S2N stimulus belonging to 77 alcoholic subjects and similarly  
64 channels of VEP for each S1, S2M, and S2N stimulus belonging to 44 control  
subjects. Note that three channels were reference ones, hence only the active 61  
channels were used from the recorded 64 channels.

## 11 **2.7. Data analysis**

13 For analyzing the electrophysiological damages caused by long-term alcohol abuse,  
15 we used two different approaches in this study; namely complexity and energy  
analyses of the VEP signals.

### 15 2.7.1. *Complexity analysis using approximate entropy*

17 In this first approach, our aim was to compare the complexity in VEP from each  
19 region between alcoholic and control subjects. The complexity analysis can provide  
21 insight to the condition of the brain of alcoholic subjects. There are many ways  
of analyzing the complexity of VEP signals namely the linear measures such as  
global field strength ( $\Sigma$ ), global frequency field changes ( $\Phi$ ) and spatial complexity  
( $\Omega$ )<sup>15</sup> and nonlinear measures such as ApEn, Hurst Exponent, Largest Lyapunov  
Exponent, and Correlation Dimension.<sup>11</sup>

23 Previously it has been shown that the electrical activity of the brain exhibits  
25 complex behavior with nonlinear dynamical properties.<sup>11</sup> Considering this fact,  
Natarajan *et al.*<sup>11</sup> suggested that using nonlinear measures would be a better  
27 approach than traditional linear methods for analyzing the complexity of brain  
signals. Hence, in this study, we focused on the commonly used nonlinear measure  
of complexity namely the ApEn.

29 ApEn is a recently developed method that measures the irregularity of a signal  
in time.<sup>15</sup> In other words, if a data point of a signal can be predicted accurately  
31 using the previous points of the signal, then the signal is considered as regular;  
whereas if the point cannot be predicted accurately, then the signal is considered  
33 as irregular.

35 The measure of irregularity of the signal in time is obtained by comparing the  
original time series with time shifted versions of itself namely embedding the signal  
in phase space. The number of previous points used in making the prediction of the  
37 next data point is the embedding dimension,  $m$ .

39 Before ApEn can be computed, two parameters must be determined; these are  
the embedding dimension,  $m$  and radial distance,  $r$  which is the tolerance of the  
measure namely noise threshold. For this study, the value of  $m$  is set to 2 and  $r$  is

8 *T. Balli & R. Palaniappan*

1 set to 15% of the standard deviation of VEP signal since it is reported that these  
2 values provide good statistical validity for ApEn.<sup>15</sup>

3 The first step for estimating the ApEn of a time series is calculating the cor-  
4 relation integral of time series. Assuming that we have the VEP signal from one  
5 channel,  $x = x(t), x(t + \tau), \dots, x(t + (N - 1)\tau)$ , which has  $N$  data points that  
6 are measured with intervals of  $\tau$ , a sequence of vectors using time delay embed-  
7 ding, with dimension  $m$ , must be constructed such that;  $y(t) = x(t), x(t + \tau), x(t +$   
8  $2 \cdot \tau), \dots, x(t + (m - 1) \cdot \tau)$ . Following this, the distance between all pairwise vectors  
9  $y(i), y(j)$  must be determined such that  $i, j = 1, \dots, N - (m - 1)$ . After that the  
10 correlation integral can be calculated by

$$11 \quad C_i^m(r) = \sum_i^{N-(m-1)} \sum_{j=i+1}^{N-(m-1)} \Theta(r - d[y(i) - y(j)]), \quad (1)$$

12 where  $\mathbf{N}$  is the length of signal,  $\mathbf{r}$  is the tolerance of the comparison,  $\mathbf{y}(i)$  is  
13 the vector in embedding space constructed from the signal,  $\mathbf{d}[\mathbf{y}(i), \mathbf{y}(j)]$  is the  
14 Euclidean distance between vectors,  $y(i)$  and  $y(j)$ ,  $\Theta(\mathbf{x})$  is the Heaviside function  
15 such that  $\Theta(x) = 1$  if  $x > 0$  and  $\Theta(x) = 0$  if  $x < 0$ .

16 After the calculation of correlation integral the ApEn( $m, r, N$ ) is obtained by

$$17 \quad ApEn(m, r, N) = \Phi^m(r) - \Phi^{m+1}(r), \quad (2)$$

18 where

$$19 \quad \Phi^m(r) = \frac{1}{N - (m - 1)} \sum_i^{N-(m-1)} \ln[C_i^m(r)], \quad (3)$$

20 with  $\mathbf{C}(\mathbf{x})$  as the correlation integral.

### 21 2.7.2. Energy analysis

22 In the second part of the analysis, we have computed energy from each channel to  
23 compare the VEP energy (power) differences between alcoholics and controls. The  
24 energy of each VEP signal is calculated using the equation below:

$$25 \quad Energy = \sum_{n=1}^N [x(n)]^2, \quad (4)$$

26 where  $\mathbf{N}$  is the total number of data points and  $\mathbf{x}(n)$  is the data at sampled point  
27  $n$ .

## 28 3. Experimental Results

29 In this section, the experimental results obtained by performing nonlinear complex-  
30 ity and energy analyses on the VEP signals will be presented.



### 1 3.1. Complexity analysis

3 The complexity of a signal gives information about the number of parallel processes  
 5 running in the brain. The increased complexity suggests that there are more parallel  
 7 processes in the brain (i.e. more level of difficulty) whereas the decreased complexity  
 9 means that the brain is in a more focused state and there are less parallel processes  
 11 in the brain.

13 In this part of the study, our aim is to show that there are regionwise differ-  
 15 ences in complexity between alcoholic and control subjects. For the comparison of  
 17 the complexity values from two groups of subjects (i.e. alcoholics vs. controls) we  
 19 generated the null hypothesis that the complexity values of each group are similar  
 21 (i.e. the complexity values are drawn from the same population) and we performed  
 23 the statistical analysis according to that null hypothesis. Initially, we analyzed the  
 25 differences between alcoholics and controls for each picture stimulus (i.e. S1, S2M,  
 27 and S2N). Then, we analyzed the pairwise differences of picture stimuli (i.e. the  
 29 differences between S1 and S2M, S1 and S2N, S2M and S2N) among alcoholics and  
 31 controls.

#### 17 3.1.1. Comparison of stimulus differences between alcoholic and control 19 subjects

21 We performed a multivariate analysis of variance (MANOVA) to compare the  
 23 regionwise complexity differences using complexity values from each region as  
 25 dependent vector. All the statistical comparisons were conducted at a confidence  
 27 level of 95% (i.e. alpha was set 0.05). The  $p$ -values smaller than or equal to 0.05  
 29 indicated that the probability that the complexity values are drawn from the same  
 31 population is very small. The test, therefore supported the alternate hypothesis  
 that there were significant differences between two groups of subjects.

Table 3 shows the results of the regionwise complexity comparison between two  
 groups of subjects. For both S1 and S2M stimuli, the complexities in all regions  
 were significantly different between alcoholics and controls where the VEP signals  
 of alcoholics exhibited higher complexity compared to controls. This could mean  
 that when the alcoholics were exposed to the visual stimuli, they had to utilize  
 more parallel processes in their brain to process the visual stimuli as compared to

Table 3. Complexity comparison between alcoholic and control subjects using approximate entropy method.

Region	S1 Picture Stimulus		S2M Picture Stimulus		S2N Picture Stimulus	
	Hypothesis	$p$ -value	Hypothesis	$p$ -value	Hypothesis	$p$ -value
Frontal	1	0.00	1	0.03	0	0.43
Temporal	1	0.00	1	0.00	1	0.00
Central	1	0.00	1	0.05	1	0.04
Occipital	1	0.00	1	0.04	1	0.02
Parietal	1	0.00	1	0.00	1	0.00

1 control subjects. The increased complexity could be the reason of the slower and  
 2 poorer quality of responses from alcoholic subjects, which were indicated in another  
 3 study.<sup>1</sup>

4 For S2N stimulus, the regions: temporal, parietal, occipital, and central, exhibited  
 5 significant difference whereas the frontal region did not indicate any significant differ-  
 6 ence between alcoholic and control subjects. The possible reason for this could be that  
 7 the S2N stimulus evokes considerable decision-making ability when compared to the  
 8 short-term memory recall, therefore the frontal region (which mediates mostly short-  
 9 term memory) may have not evoked enough complexity to differentiate the groups  
 during S2N stimulus; thereby indicating no significant difference in frontal region.

### 11 3.1.2. *Pairwise stimuli difference among control and alcoholic subjects*

12 We performed several MANOVA tests among control and alcoholic subjects to  
 13 compare complexity values evoked by different stimulus conditions, i.e. S1 and S2M,  
 14 S1 and S2N, S2M and S2N. Similar to the previous case, the statistical comparisons  
 15 were conducted with a confidence level of 95% where  $p$ -values smaller than or  
 16 equal to 0.05 indicated that there were significant differences between two groups  
 17 of stimulus conditions.

Table 4. Complexity comparison of picture stimulus among alcoholic and control subjects using approximate entropy method.

Region	Alcoholic Subjects		Control Subjects	
	S1&S2M Picture Stimulus		S1&S2M Picture Stimulus	
	Hypothesis	$p$ -value	Hypothesis	$p$ -value
Frontal	1	0.01	1	0.05
Temporal	1	0.01	1	0.01
Central	1	0.00	1	0.00
Occipital	0	0.38	0	0.56
Parietal	0	0.52	0	0.19
Region	S1&S2N Picture Stimulus		S1&S2N Picture Stimulus	
	Hypothesis	$p$ -value	Hypothesis	$p$ -value
	Frontal	0	0.12	0
Temporal	0	0.34	0	0.20
Central	1	0.00	1	0.00
Occipital	0	0.27	0	0.66
Parietal	0	0.96	0	0.68
Region	S2M&S2N Picture Stimulus		S2M&S2N Picture Stimulus	
	Hypothesis	$p$ -value	Hypothesis	$p$ -value
	Frontal	0	0.68	0
Temporal	0	0.18	0	0.55
Central	0	0.87	0	0.53
Occipital	0	0.98	0	0.68
Parietal	0	0.89	0	0.69

1 Table 4 shows the results of comparison among control and alcoholic subjects  
 2 using ApEn. As it could be seen from the table, region differences were similar  
 3 among alcoholic and control subjects for all of the stimuli pairs.

4 When the subjects were exposed to S1, recognition and memory encoding takes  
 5 place whereas when they were exposed to the S2M or S2N, memory access and  
 6 decision-making processes are evoked. Both groups of subjects indicated signifi-  
 7 cantly higher complexity for S2M as compared to S1 in frontal, temporal, and  
 8 central regions. This denotes more complexity in these regions during memory  
 9 retrieving and comparing the matching stimulus. When the subjects were exposed  
 10 to S2N, only the central region indicated higher complexity which could denote that  
 11 nonmatching stimulus (being easier to decide the mismatch and in some manners,  
 12 similar to S1 like seeing a new picture) does not involve more complexity in most  
 13 parts of the brain as compared to S1. When S2M and S2N were compared, the  
 14 results indicated no differences in any region since these cognitive processes evoke  
 15 similar amount of complexity.

### 3.2. *Energy analysis*

17 In the second part of the analysis, energy (power) of the VEP signals between  
 18 alcoholics and controls were compared. Similar to complexity analysis, we initially  
 19 compared the picture stimulus (i.e. S1, S2M, S2N) energy differences between alco-  
 20 holic and control subjects and then we compared the differences in pairwise stimuli  
 21 among alcoholic and control subjects.

#### 3.2.1. *Comparison of stimulus differences between alcoholic and control subjects*

23 For comparison of regionwise energy values between alcoholic and control subjects,  
 24 the same MANOVA analyses as complexity analysis between two groups of subjects  
 25 were carried out.

27 Table 5 shows the regional energy comparison between alcoholic and control  
 28 subjects. The results indicate significant differences between energy of alcoholic  
 29 and control subjects for all of the regions regardless of the type of picture stimulus.  
 As a result of this analysis, we could easily conclude that the alcoholic subjects

Table 5. Energy comparison between alcoholic and control subjects.

Region	S1 Picture Stimulus		S2M Picture Stimulus		S2N Picture Stimulus	
	Hypothesis	<i>p</i> -value	Hypothesis	<i>p</i> -value	Hypothesis	<i>p</i> -value
Frontal	1	0.04	1	0.01	1	0.02
Temporal	1	0.00	1	0.00	1	0.00
Central	1	0.00	1	0.03	1	0.01
Occipital	1	0.00	1	0.00	1	0.00
Parietal	1	0.00	1	0.00	1	0.00

1 exhibited a decreased energy level as compared to control subjects for all regions  
 2 of the brain. These decreased energy levels in alcoholic subjects could be due to  
 3 the impairments in the information processing capacity of the brain caused by  
 long-term alcohol abuse.

### 5 3.2.2. *Pairwise stimuli difference among alcoholic and control subjects*

6 Similar to the pairwise stimuli comparison among two groups of subjects using  
 7 complexity values, we performed several MANOVA tests to compare regionwise  
 energy values evoked by different stimulus conditions, i.e. S1 and S2M, S1 and  
 9 S2N, S2M and S2N.

10 Table 6 shows the results of pairwise stimuli comparison among alcoholic and  
 11 control subjects. Control subjects indicated differences for frontal, central, and tem-  
 poral regions while alcoholics indicated differences for all parts of the brain for S1  
 13 and S2M stimuli comparison. It is known that mental processing of a visual stimulus  
 results in fast sensory reception occurring in visual cortex (occipital lobe) followed  
 15 by slower cognitive activity in frontal and parietal lobes (short-term memory recall  
 and cognitive processing of stimulus).<sup>5</sup> Assuming that there are no impairments in  
 17 information processing for control subjects, the possible reason for differences in  
 energy of S1 and S2M for alcoholic subjects in occipital and parietal regions could

Table 6. Energy comparison of picture stimulus among alcoholic and control subjects.

Region	Alcoholic Subjects		Control Subjects	
	S1&S2M Picture Stimulus		S1&S2M Picture Stimulus	
	Hypothesis	<i>p</i> -value	Hypothesis	<i>p</i> -value
Frontal	1	0.00	1	0.00
Temporal	1	0.00	1	0.00
Central	1	0.00	1	0.00
Occipital	1	0.00	0	0.27
Parietal	1	0.00	0	0.09
Region	S1&S2N Picture Stimulus		S1&S2N Picture Stimulus	
	Hypothesis	<i>p</i> -value	Hypothesis	<i>p</i> -value
	Frontal	1	0.00	1
Temporal	1	0.00	1	0.00
Central	1	0.00	1	0.00
Occipital	1	0.00	0	0.20
Parietal	1	0.00	1	0.01
Region	S2M&S2N Picture Stimulus		S2M&S2N Picture Stimulus	
	Hypothesis	<i>p</i> -value	Hypothesis	<i>p</i> -value
	Frontal	0	0.52	0
Temporal	0	0.65	0	0.24
Central	0	0.26	0	0.95
Occipital	0	0.41	0	0.76
Parietal	0	0.93	0	0.72

1 be that when the alcoholic subjects were exposed to the second picture, the energy  
of these regions increase due to impairments in cognitive processing at these regions  
3 while they are trying to compare S2M to S1.

5 In a similar fashion, alcoholic subjects indicated differences for all regions while  
controls indicated differences in all regions except for occipital (visual cortex) for  
7 S1 and S2N stimuli comparison. Here when the subjects are exposed to first and  
second nonmatching stimulus only occipital region is invoked as they respond both  
of the stimulus as a new incoming visual stimulus. Similar to the previous case the  
9 alcoholics had increased energy in the occipital region when they were exposed to  
second nonmatching stimulus possibly due to deficits in mental processing activity  
11 at alcoholic subjects.

13 When S2M and S2N were compared, the results indicated no differences in any  
region.

#### 4. Discussion

15 Conventionally the validity of applying nonlinear dynamic methods to EEG should  
be investigated using surrogate data method as suggested by Kaplan *et al.*<sup>16</sup> Sur-  
17 surrogate time series are artificially generated time series that retain the linear prop-  
erties of original signal.<sup>16,18</sup> Basically this method is used to confirm the presence  
19 of nonlinear dynamics in the biological signals (for example EEG and ECG<sup>16,17</sup>).  
For testing the nonlinearity, a discriminating statistic should be selected to extract  
21 the test statistics of original and surrogate data and perform rank based *t*-test to  
accept or reject the null hypothesis of linearity. There are lots of test statistics that  
23 can be used to test linearity such as delay vector variance method,<sup>17</sup> correlation  
dimension,<sup>16</sup> and nonlinear prediction error.<sup>16</sup> Detecting nonlinearity or linearity  
25 of signals allows us to know if the utilized analysis techniques are appropriate. In  
the present study, the presence of nonlinear structure in the EEG signals was not  
27 investigated before actual nonlinear complexity analysis which could be considered  
as a limitation of our study.

29 In this study, we have investigated the complexity and the energy of VEP signals  
to analyze the electrophysiological differences between alcoholic and control sub-  
31 jects. We have shown that there are significant differences in complexity between  
alcoholic and control subjects in almost all regions of the brain in which the com-  
33 plexity of alcoholic subjects are higher compared to control subjects. This can be  
due to the effects of long-term alcohol abuse. When we considered the differences  
35 between pairs of picture stimuli among alcoholic and control subjects, the results  
indicated that frontal, temporal, and central regions becomes more complex during  
37 S2M as compared to S1 whereas the results also indicated that the central region  
becomes more complex during S2N as compared to S1. These were true for both  
39 alcoholic and control subjects.

41 The energy analysis indicated that there are significant differences between alco-  
holics and controls in which the VEP signals of control subjects exhibit more energy

1 compared to alcoholic subjects. Again, this could be due to the impairments in  
2 cognitive processing capacity of alcoholic subjects. Considering the pairwise stimuli  
3 differences among alcoholic subjects, the results indicated that the VEP signals  
4 exhibit more energy during S2M and S2N as compared to S1 in all regions. When  
5 the control subjects were considered, higher energy was indicated only in frontal,  
6 temporal, and central regions in the case of S2M compared to S1 and in frontal,  
7 temporal, central, and parietal regions in the case of S2N compared to S1.

8 As a conclusion; for both energy and complexity analysis between alcoholic  
9 and control subjects, the results of this study showed that there are differences  
10 mostly in occipital, parietal, and frontal lobes. These parts of the brain are known  
11 to evoke when perception and cognitive processing of a visual stimulus occurs.<sup>8</sup>  
12 These differences in complexity and energy between alcoholic and control subjects  
13 indicate that there are impairments in cognitive processing of alcoholic subjects  
14 due to long-term alcohol abuse.

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