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Electroencephalography (EEG) Analysis of Alcoholic and Control Subjects Using Multiscale Permutation Entropy

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***Abstract*—Brain electrical activity as reflected in Electroencephalography (EEG) have been analyzed and diagnosed using various techniques. Among them complexity measure, nonlinearity, disorder and unpredictability play vital role due to nonlinear interconnection between functional and anatomical subsystem emerged in brain in healthy state and during various diseases. There are many social and economical issues of alcoholic abuse as memory weakness, decision making, impairments and concentrations etc. Alcoholism not only defect the brains but also associated with emotional, behavior and cognitive impairments damaging the white and gray brain matters. A recently developed signal analysis method i.e. Multiscale Permutation Entropy (MPE) is proposed to estimate the complexity of long-range temporal correlation time series EEG of Alcoholic and Control subjects acquired from University of California Machine Learning repository and results are compared with MSE. Using MPE, coarsed grained series is first generated and the PE is computed for each coarsed grained time series against the electrodes O1, O2, C3, C4, F2, F3, F4, F7, F8, Fp1, Fp2, P3, P4, T7 and T8. The results computed against each electrode using MPE gives higher significant values as compared to MSE as well as mean rank differences accordingly. Likewise, ROC and Area under the ROC also gives higher separation against each electrode using MPE in comparison to MSE.**

Keywords—Electroencephalogram (EEG), Multiscale Permutation Entropy (MPE), Multiscale Sample Entropy (MSE), Permutation Entropy (PE), Mann Whitney Test (MMT), Receiver Operator Curve (ROC), Complexity Measure.

1. INTRODUCTION

Since its discovery, the Electroencephalography (EEG) has been widely used to examine the neuropathology through a noninvasive physiological to monitor the patients. The EEG is a well-established modality to measure the electrical activity generated by populations of neurons of the cerebral cortex. According to the international 10-20 system, the bioelectric signals are recorded through a set of scalp electrodes by properly placing over the head. The EEG is essentially a multichannel data collection representing information connected with the brain activities: from an information processing perspective, it represents indeed anon-stationary, multivariate, nonlinear time series. Many authors are of the opinion that the concept of entropy has achieved a large consent as an indicator of complexity of nonlinear signals [1].

An important nature of EEG in its dynamics represents 'complexity', characterized quantitatively by complexity analysis. Complexity analysis is a nonlinear technique characterizing whether acupuncture affects the complexity and what the effect is. Lempel and Ziv developed the most popular complexity measure as LZ complexity. Other prevalent complexity measures includes spectral entropy, approximate entropy, spectral entropy and median frequency where LZ complexity measure C(n) can act as an alternative tool for EEG analysis, since it is suitable to characterize the development of spatiotemporal activity patterns in high-dimensionality nonlinear systems like heart and brain [2].

There are millions of neurons in human brain producing electric voltages field for each cerebral activity. The EEG signal in normal adult ranges from 1 to 100 microvolts, when recorded and measured from electrodes placed on scalp. Many researchers analyze EEG signals measured under different mental conditions such as dementia, Alzheimer disease, epilepsy, alcoholic and drowsy states. S. N. M. Ashtiani and Z. Mardi worked on EEG based drowsiness detection methodology for driving safely, using chaotic features of EEG data. Likewise, R.U. Acharya and O. Faust classify and analyzed EEG signals recorded during epileptic, controlled, and alcoholic states using AR modeling techniques. While, M. Rangaswamy and B. Porjesz used beta power estimation to analyze EEG alcoholics subjects [3].

The recorded physiological signals are nonlinear, space varying, time varying and nonstationary in nature. Nonlinear dynamical analysis can provide complementary information about the dynamics under psychological or physiological states compared with classical linear time series analysis methods such as spectral or Fourier analysis. Nonlinear dynamical analysis techniques have been derived from theory of nonlinear dynamical systems such as Lyapunov exponents, the correlation integral and correlation dimension recently used in a number of fields of

application. Complexity analysis is one of the nonlinear estimation of dynamical EEG, EOG, and EMG activity. Entropy based algorithm is robust and widely been used estimator for complexity analysis to evaluate the predictability and regularity. In wavelet domain, Shannon entropy (SE) is used to measure the flatness of energy spectrum. Approximate entropy (ApEn) and its refined version sample entropy (SampEn), were developed as practically good physiological measures robustness to noise and finitude of data sets and applicable to nonlinear deterministic, stochastic and composite processes. Lempel–Ziv complexity (LZC) approach is used such problems that links the complexity of a specific sequence to gradually buildup new patterns along the given sequence [4].

Moreover, EEG signals can be considered as an output of a highly non-linear multidimensional system. Researcher from past two decades used chaos and nonlinear theory methods to follow transition from interictal to ictal period. Such studies have focused on measures like the correlation dimension, Lyapunov exponents, fractal dimensions and entropy measures. EEG signals are generally nonstationary and these methods generally require long and stationary data for analysis [5].

The concept of entropy has achieved a large consent as an indicator to measure the complexity of nonlinear signals. A variety of notion has been proposed in the literature to show different degrees of flexibility, efficiency in their computation, relevance to different problems, as well as theoretical foundations. The information processing in the brain manifests itself through its global electrical activity, measured by the electroencephalogram (EEG) which is multidimensional, nonlinear and non-stationary time series. This assumption is at the basis of the study of EEG through entropy aims to extract information that is useful to distinguish among different brain states such as normal and pathological aging detected by means of complexity analysis. The complexity is lost under stress due to aging and related diseases. Permutation Entropy (PE) has been introduced as a fast and robust method to extract information from time series especially for complexity analysis. PE is based to count the ordinal patterns (called “motifs”) that illustrate the up-and-down in the dynamical signal. Moreover, PE is measure of relative frequencies having different motifs. The amplitude of signals is not relevant as ordinal patterns are just considered thus yielding a structural robustness to noise. Accordingly, there is no need of the usual normalization and pre-processing step. As an invariant measure, PE is expected to quantify the complexity of the system from time series, by discerning the relative change of complexity from limited amount of data [6].

Alcoholism has the third largest impact on physical ability and human health. Chronic drinking can cause alcohol-related brain damage (ARBD), including brain structure changes, which humiliating as white matter deficits, grey matter change, mild brain atrophy, corpus callosum, atrophy frontal system damage and brain cognitive function damage which includes working memory deficits, a weakened capacity, executive function damage for processing complex information and an impaired sense of smell. Moreover, chronic alcohol abuse can cause starvation and liver dysfunction resulting serious diseases, such as Korsakoff syndrome and Wernicke encephalopathy [7].

To investigate the EEG several methods based on nonlinear theory have been developed including lyapunov exponent, correlation dimension, entropy, dissimilarity measures and recurrence quantification analysis. Pompe and Bandt in 2002 introduced the concept of ordinal patterns to describe the order relations between the values of a time series. This novel complexity based measure was named permutation entropy (PE) used to quantify the diversity of these patterns. It was observed that PE detects changes in the dynamics underlying nonlinear time series data. Permutation entropy is computationally very fast and robust with respect to noise [8]. PE was recently introduced to the temporal analysis of absence seizure EEG , to epileptic EEG and to the study of anaesthesia drug effects [9].

Claude Shannon introduced the term ’entropy’ in the field of information technology in one of his classic paper on communication theory. This measure, extensively known as Shannon entropy, is computed by applying the Shannon equation to the probability distribution of the variable under concern, however, Approximate entropy (ApEn) and Sample entropy (SmpEn), are based on the phase space representation of the time series. Permutation entropy (PrmEn), on the other hand, quantifies the occurrences of patterns in the time series [10].

Using permutation entropy, the value of PE increased for large lags nearly reaching 1 after some lags. This holds true for EEG signals from both epileptic and healthy subject patients. From the theory behind PE it is known that PE=1 indicating noise-like signals. This implies that EEG samples become samples of stochastic signal for lag larger than some critical value and PE might not make sense. Likewise, the change in lag also affects the time duration of each pattern, so there is a relationship between sampling rate and PE for particular signal. Some optimal combination of values of entropy order, sampling frequency and pattern lag might be selected for which PE is meaningful; otherwise it is meaningless [11].

To measure the complexity of a finite length time series a new method Multiscale analysis is used. Single-scale entropy measures quantify only the regularity of the time-series: one typical disadvantage of this approach is that this measure tends to yield lower entropy in time series of physiologic data than in surrogate series formed by shuffling the original physiologic data. Indeed, the shuffled data are less

ordered than the original series that typically contain correlations at many time scales. Surrogate data show reduced correlations and degradation of the information content of the signal: this is ambiguous, since greater entropy should be indicative of greater complexity. In comparison, the multi-scale method demonstrate that the original time series are more complex than the surrogate ones, by illuminating the dependency of entropy measures on the scale [12].

Presently, the researchers are investigating the influence of alcohol to the brain and literatures illustrate the impact of alcoholism on several components of the event related potential (ERP). Porjesz and Begleiter's in their study on 1996 reported the most commonly ERP deficit in alcoholics is the reduced amplitude of P300 for the task relevant target stimuli during oddball tasks. It has been suggested that ERP components are the end products of specific superposition of oscillations in various frequency bands, and P300 consists primarily of delta and theta oscillations. Evoked theta and delta power are significantly reduced and observed in alcoholics while processing the target stimuli in a visual oddball paradigm, indicating that the reduced P300 amplitudes reported in alcoholics are caused by deficits in theta and delta oscillations that underlie P300 [13].

Like many other complex traits, alcoholism remains a challenge to those trying to categorize individuals as either affected or normal. In alcoholics, grey and white brain matter is damaged. In alcoholic subjects, the white and grey matters are reduced in comparison to non-alcoholic subjects. Due to these damages the functional connectivity in alcoholic may be disturbed between distinct brain regions. Functional connectivity can be evaluated to determine the synchronizations between electrical activities in different brain areas. The impairments could cause accidents especially in certain jobs like machine operation and driving, where it is important to be helpful and to be able to make good assessment and decisions. Therefore, it becomes important to devise some methods that discriminate alcoholics, alcohol abusers from the rest of population. An automated method will help the psychiatrists to classify the alcoholics [14].

Alcoholism is one of psychiatric phenotypes influenced by environmental and genetic factors. It not only defect the brain but also associated emotional, cognitive and behavioral abnormalities. The effects of short and long term of alcohol on various organs of body have been studied mostly in human brain. A number of the studies reveal the harmful effect of alcohol on nonalcoholic offspring of alcoholics. To study the change in EEG activity and structural changes in human brain of long term abstinent alcoholics both invasive and noninvasive techniques have been used. Even though invasive technique like Trans cranial Magnetic stimulation (TMS) and some of the noninvasive techniques such as Magnetic Resonance Imaging (MRI), Computed Tomography (CT), Positron Emission Tomography (PET) and functional MRI activated Electroencephalography (EEG) have been used to study the harmful effects of alcohol abuse and dependence EEG by itself still seems to be an important tool for brain study. Various frequency domain, time domain, time-frequency domain, chaotic signal processing, parametric methods, and statistical techniques have been used to characterize EEG/ERP signals in alcoholics and healthy controls .Many studies concentrated upon the estimation of entropies as a measure of the complexity of EEG signal. Entropy estimation provides important information regarding the complexity of the process involved in terms of the width of the spectrum [15].

2. PROPOSED METHODS

2.1 EEG Recordings

In this study 58 subjects are taken consisting of 29 from alcoholic group and 29 from that of the control group available at Machine learning repository UCI database. EEG signals are extracted from 14 electrodes – C3, C4, F3, F4, F7, F8, Fp1, Fp2, O1, O2, P3, P4, T7 and T8 complying with the international 10-20 system. EEG data were sampled at 256 HZ.

Entropy

The entropy was conventionally used in information theory and thermodynamics. Shannon in 1948 proposed entropy to quantify and characterize the information buried in the data thus employed broadly to measure the orderliness and regularity of a time series. Generally, the entropy increases for degree of disorder and maximum for random system. Moreover, entropy is also used to extract features for biological and physiological systems, disease diagnosis and quantifying machine fault detection. Consider a single random series S having N outcomes with n classes, the entropy En(S) can be mathematically defined as:

$$En(S) = -\sum_{i=1}^{n} p(S_i)\log\left(p(S_i)\right), S_i \in S, 1 \le i \le n$$

Where $p(S_i)$ represent the probability density function of random series S. Generally, entropy is applied to measure the complexity of random variable series to predict its behavior.

Permutation Entropy

Bandt et al. in 2002 proposed permutation entropy to measure and quantify the quality of irregularity and complexity of a system. PE is also employed to analyze the EEG signals. Permutation entropy is based on Shannon entropy and is computed by calculating the probability density function of time series in specific order.

Multiscale Permutation Entropy

A technique to measure the complexity of a time series using entropy based method implies that random sequences accomplish maximal complexity. In comparison, the complexity analysis can be faced from a "structural" viewpoint: the complexity should not be maximum neither for completely random sequences nor for completely regular. In physiological and biological time series, there are often underlying structural or evident correlations over multiple spatial-temporal levels (scales). Among many other measures, Multi-Scale Entropy (MSE), proposed in 2002 by Costa et al shown to be one of the most effective methods that explicitly accounts for such structural effects at multiple time scales present in complex real data. MSE yields a systematic procedure to associate to both fully predictable and uncorrelated random signals a small value of complexity. In contrast, correlated processes show high complexity over different scales. MSE is a method of measuring the complexity of finite length time series that can be appropriately used with different types of entropic measures. In [14], the Sample Entropy formulation has been used. Here, we propose to use MSE for evaluating at multiple scales the previously introduced PE. We will limit our analysis from single scale to scale four because of the limited size of the available recordings. As a matter of fact, for PE, a possible way to explore correlations among different scales could be the proper variation of the time lag parameter, τ. However, it is our opinion that the MSE procedure is easier to interpret with respect to the direct variation of τ, which implies a fictitious frequency dependence on the sampling frequency. Thus, the usual coarse-graining procedure is implemented, as follows [6].

Aziz and Arif in 2005 proposed Multiscale Permutation Entropy (MPE) to measure the entropy of physiological signals. Following steps are used to compute the MPE:

Step 1:

Considered a discrete time series $\{ X_i, i = 1,2,3,4, \dots \dots \dots, N\}$, by averaging the data points within non overlapping windows of increasing length, multiple coarsed grained times series have been constructed using the following equation:

$$y_j^{(\tau)} = \frac{1}{\tau} \sum_{i=(j-1)\tau+1}^{j\tau} x_i \ , 1 \le j \le \frac{N}{\tau}$$

Where τ represents the scale factor and length of each coarsed grained series is equal to original time series divided by τ.

Step 2:

Following procedure is used to compute the permutation entropy

Consider a coarsed grained time series $Y_j, j = 1,2,3, \dots ., M\}$ which is embedded to m dimensional space.

$$Y_j - [y(j), y(j + L), \dots \dots ., y(j + (m - 1)L)]$$

Where m is embedding dimension and L is time delay. For each j, m dimensional number of real value $Y_j - [y(j), y(j + L), \dots \dots ., y(j + (m - 1)L)]$ can be arranged in increasing order

$$[y(j + (j_1 - 1)L \le y(j + (j_2 - 1)L, , , , , , , , , \le y(j + (j_m - 1)L]$$

To uniquely mapped any vector Y_j onto $(j_1, j_2, j_2, , , , , , , j_m)$ we require m! permutations of m distinct symbols [1,2,3,….,m]. Consider the probability distribution for distinct symbols $P_1, P_2, P_3, , , , , , P_k$ where $k \le m!$, permutation entropy for coarsed grained time series defined as Shannon entropy is computed as:

$$H_p(m) = -\sum_{i=1}^{k} P_i \ln P_i$$

$$\text{For } P_j = \frac{1}{m!}, H_p(m) \text{ attains maximum value of } \ln(m!)$$

3. RESULTS

Table 1: Average slope values of the MPE and *MSE* profiles for time scales (t ≤ 10) of the EEGs for Alcoholic and Control groups for all channels with *m* = 1 and *r* = 0.25 times the standard deviation of the original data sequence using Mann-Whitney-Wilcoxon non parametric test

Electrode	MSE			MPE			
	Mean Rank		P-value (Max. Separation)	Mean Rank		P. value (Max. Separation)	ROC
	Alcoholic	Control		Alcoholic	Control		
C3	18.63	41.14	7.00E-08	15.41	43.59	2.11E-10	0.978
C4	19.27	40.46	1.80E-07	15.00	44.00	3.26E-11	0.996
F3	23.03	36.43	8.40 E-04	20.26	38.74	1.65E-05	0.813
F4	27.70	31.43	0.337	21.93	37.07	7.00 E-04	0.756
F7	23.87	45.54	1.56 E-03	16.66	42.34	7.24E-09	0.936
F8	21.70	37.86	2.60E-05	14.16	42.86	8.81E-10	0.961
Fp1	28.20	30.89	0.183	21.00	38.00	6.52E-05	0.791
Fp2	27.77	31.36	0.122	24.29	34.71	9.83 E-03	0.647
O1	21.23	38.36	4.70E-05	19.52	39.48	3.49E-06	0.830
O2	24.73	34.61	0.0116	20.14	38.86	1.25E-05	0.814
P3	20.77	38.86	5.80E-06	21.97	37.03	3.49E-04	0.736
P4	26.70	32.50	0.067	21.90	37.10	3.12 E-04	0.757

T7	20.23	39.43	2.20E-05	19.62	39.38	4.34E-06	0.837
T8	26.68	32.13	0.0496	22.50	36.50	8.41 E-04	0.739

The Table 1 depicts the significant difference were obtained at all the electrodes from scale 1 to 10 using both MPE and MSE and maximum separation (p-value<0.005) was obtained. However, MPE gives more significant p-value for all electrodes than MSE profile. Most of the frontal region electrodes discriminate the alcoholic subjects from control that will help the neurologist to use frontal, central and parietal electrodes to examine the Eye Alcoholism affects for pathological and clinical examinations.

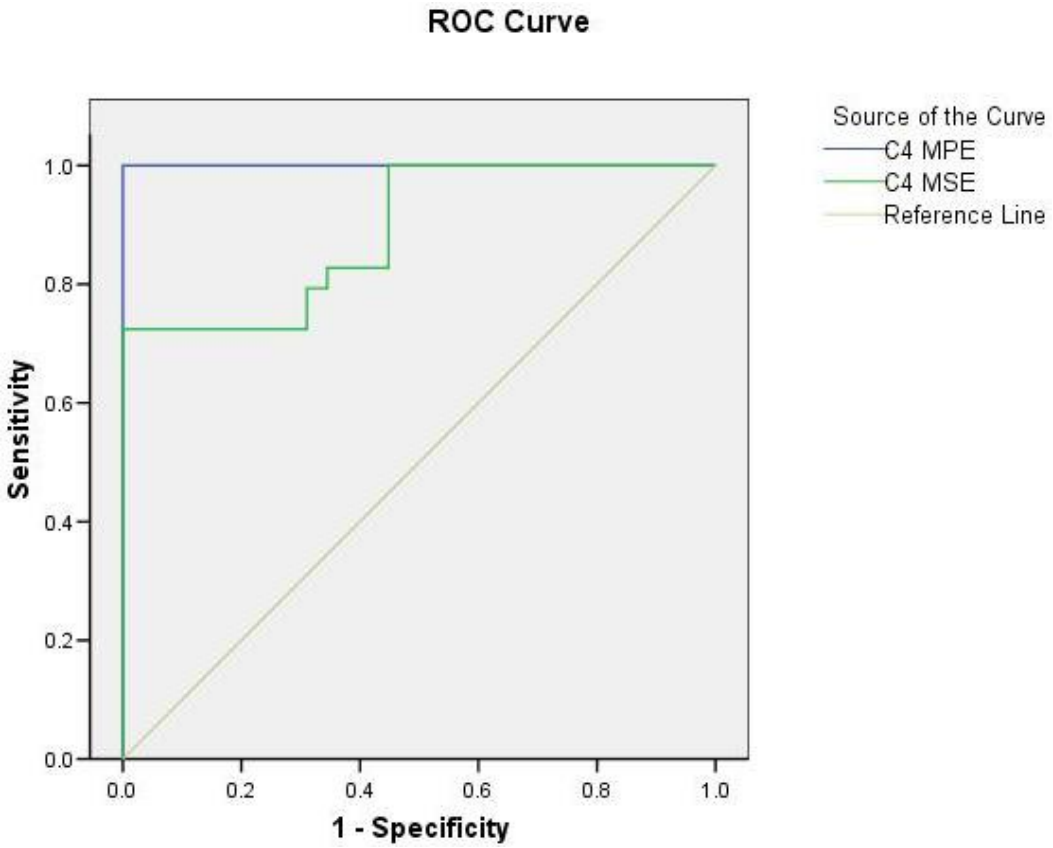

Figure: ROC at Electrode C4 using MPE and MSE; AUC =1.00 using MPE and AUC=0.889 using MSE

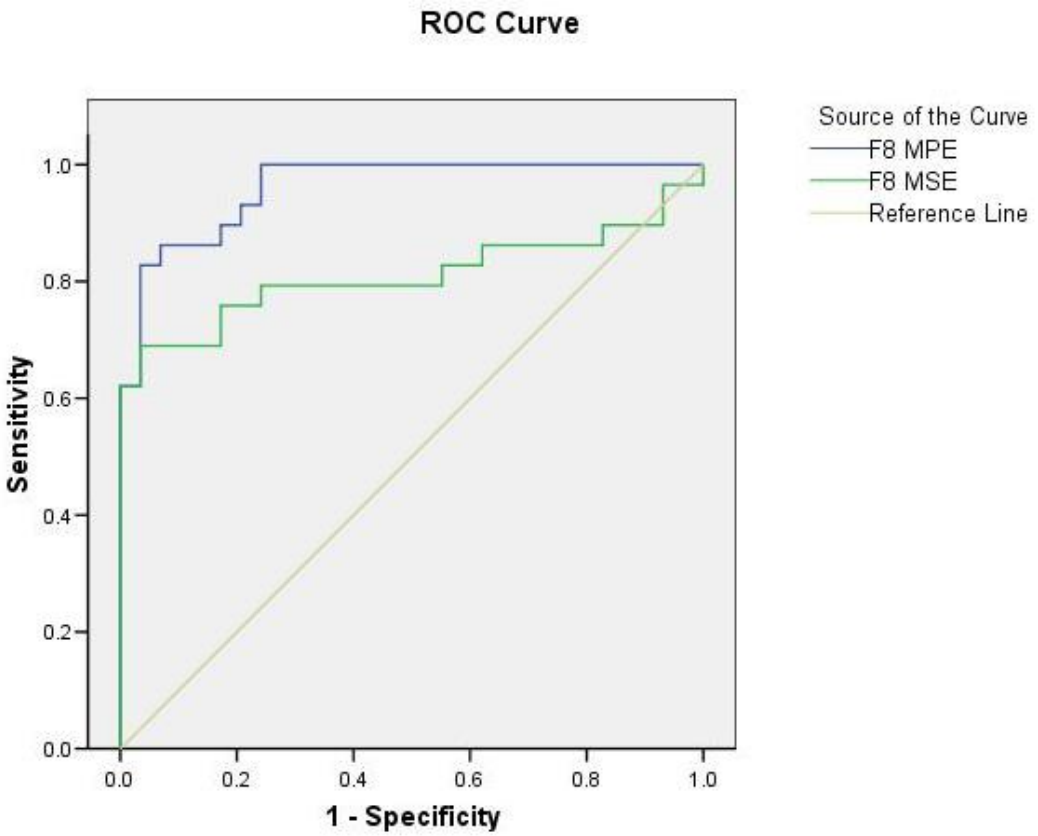

Figure: ROC at Electrode F8 using MPE and MSE; AUC =0.961 using MPE and AUC=0.810 using MSE

4. DISCUSSIONS

The data analyzed so far is obtained from University of California Machine Learning repository from 58 subjects: 29 from patients affected by alcoholic and 29 from normal subjects (control). EEG recordings are obtained using 10-20 international system. A coarsed grained series is generated and PE is computed for each coarsed grained series for both entropy based MPE and MSE techniques. It was seen that healthy subjects presents greater PE values than alcoholic subjects at all time scales against each channel. This is because; alcoholic subjects have been characterized by increased predictability because during alcoholism white and gray neurons synchronously discharged that is also reported by (Labate et al. 2013) in the patients suffered from epileptic seizure.

From results it is also observed that PE values at higher scales does not change too much between healthy and control subjects. Moreover, using both MSE and MPE it is indicated that difference between alcoholic and control subjects at scale 1 to 5 is more evident and decreases by increasing scale factor because of the fact that alcoholic subjects are being averaged by using coarsed graining process. Likewise, the electrodes C3, C4, F8, Fp1, Fp2, O1, O2, P3, P4, T7 and T8 gives maximum separation at different time scales such as scales 1,1,2,2,3,3,2,1 and 5 respectively. In addition, for both alcoholic and control groups at all the electrodes the differences were analyzed using Mann Whitney t test (Rank sum method) as shown in Table 1. Using MSE the significant differences were not found at electrodes F4, Fp1, Fp2 and P4 in both normal and alcoholic groups, while other all electrodes depicts the significant differences, however MPE has given highly significantly results at each electrodes including F4, Fp1, Fp2 and P4. Thus MPE is to be considered more robust in discriminating alcoholic groups from that of control groups. The literature also reveals to discriminate normal groups from pathological groups using various nonlinear dynamical studies including L1, D2 and A-CMI (Na et al. 2002, Elbert et al., 1992; Koukou et al., 1993). The results obtained in this study are also consistent with these previous studies using entropy based nonlinear techniques to distinguish alcoholic subjects from control subjects. Previous studies also exhibits that patients having depression suffer from neuropsychological deficit in attention, psychomotor speed, memory, processing speed and execution function (Gaultieri et al., 2006) These studies using nonlinear analysis of EEG also depicts that averaged global entropy slightly decreasing with the treatment of patients (Thomassen et al., 2000). Overall, it was observed that central region (C3, C4), Frontal region (F3, F4, F7, F8, Fp1, Fp2), Parietal region (P3, P4) and Occipital region (O1, O2) has given good separation using MPE. Thus these electrodes in these regions will be helpful to the neurologist and physicians to improve the deficit in different brain lobes to process information for psychiatric and drug addicted patients. Maximum significant results were obtained in central frontal and temporal areas which were consistent with other studies (Allen et al, 2004; Na et al, 2002; Vuga et al, 2006). Table 1 also depicts the statistical outcomes of linear complexity analysis between pathological and

control groups. Out of 14 electrodes it was found that electrodes C4, C4, F8 depicted the highest separation between these groups using MPE. From the results it is also evident that control subjects at all these channels exhibits higher complexity than alcoholic due to the fact that complexity decreases in alcoholic subjects due to die in white and gray cells neurons while out of 16 channels only few channel fails to distinguish these groups using MSE while MPE has significantly distinguish these groups at all 16 electrodes.

Moreover (Pezard et al, 1969) represented that depressive subjects shows low level of linear complexity than control subjects. Besides, computing other complexity measures (Wackerbauer et al, 1994) provide a more comprehensive overview of underlying process. The advancement in theory of nonlinear dynamics has provided new methods to study EEG one of them is entropy based computation which addresses the randomness and predictability showing that greater entropy values is often associated with more randomness and less system order.

In this study, we discussed the EEG Motor Movement/ Imagery data comprising of Baseline Eye open and Eye close tasks using MSE which can assess the signal complexity and compute the regularity of coarse-grained sequence at different time scales. MSE as proposed by Costa et al 2005 was used for small data of one to two minute EEG recording of Motor Movement has important advantage with other traditionally used non-linear techniques such as L1, D2 as it can be applied relatively noisy and short physiological time series and model independent. Moreover, MSE can be applied to measure complexity of physiological and pathological subjects on different time scales (Costa et al 2005).

By comparing the results of MSE and MPE, we realized that MPE analysis has provided statistically significant differences in more electrodes using 10-20 system than MSE method, whereas MSE method has advantage over traditionally used nonlinear techniques such as D2, L1, SampEnt, ApproxEnt and is model independent (Costa et al 2005). Moreover, using MPE the accuracy and ROC values found to be higher than correspondence values of MSE as depicted in Table 1 and Figures 1 and 2. For example MPE was to differentiate electrodes from control subjects with ROC values higher than 0.90 at four electrodes (C3, C4, F7, F8) and ROC values higher than 0.80 to 0.90 at four electrodes (F3, O1, O2, T7). In contrast, MSE method has not provided ROC values greater than ROC values of MPE method. To sum up, it was found that MPE gives significant differences between alcoholic and control subjects all 14 electrodes (C3, C4, F3, F4, F7, F8, Fp1, Fp2, O1, O2, P3, P4, T7 and T8). Moreover, MSE and MPE analysis reveals that alcoholic patients usually have lower complexity at smaller time scales at most of the electrodes of 10-20 system. Thus it can be inferred that brain activities are considered less complex in alcoholic groups than control groups agree with the previous studies results (Costa et al 2005, Besthorn et al 1995, Jelles et al 1999, Jeong et al 1998, 2001 a, Stam et al 1995) and less regular (Abasolo et al 2005, 2006 a,b) in EEG recordings of pathological patients than control patients. Thus it can be further inferred that lower complexity in alcoholic subjects might be due to the extensive of neuronal death, neurotransmitter deficiency and decrease in local neural network connection due to the death of nerve cell (Jelles et al 1999, Jeong et al 2004, Tononi et al 1998).

5. CONCLUSION

In the present study, electroencephalography (EEG) background activity in patients having alcoholism have been investigated using nonlinear entropy based computational novel techniques. MSE and MPE were applied to discriminate the alcoholic subjects from control subjects at 14 electrodes of 10-20 international system. A coarsed grained series is first generated for all the electrodes and PE and SE are computed against each coarsed grained series. The significance (p-value) was computed against each electrode using MPE and MSE, showing MPE gives higher statistically significance results, higher accuracy and ROC area value than MSE. While using MSE profile some electrodes also exhibit no significant results as depicted in Table 1. Thus novel MPE method is suggested to be more powerful tool to distinguish the pathological groups from control groups which has same resemblance with the previous studies. The results also show that pathological subjects have lower complexity than control due to the neuronal death and decrease in the local neuron connection.

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