2015-08

Tsallis entropy as a biomarker for detection of Alzheimer's disease

Al-Nuaimi, Ali H. Husseen

10.1109/embc.2015.7319312
2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)
IEEE

Tsallis Entropy as a Biomarker for Detection of Alzheimer's Disease

Ali H. Al-nuaimi, *Student Member, IEEE*, Emmanuel Jammeh, Lingfen Sun and Emmanuel Ifeachor

***Abstract*— Alzheimer's disease (AD) and other forms of dementia are one of the major public health and social challenges of our time because of the large number of people affected. Early diagnosis is important for patients and their families to get maximum benefits from access to health and social care services and to plan for the future. EEG provides useful insight into brain functions and can play a useful role as a first line of decision-support tool for early detection and diagnosis of dementia. It is non-invasive, low-cost and has a high temporal resolution. The functions of brain cells are affected by damage caused by dementia and this in turn causes changes in the features of the EEG. Information theoretic methods have emerged as a potentially useful way to quantify changes in the EEG as biomarkers of dementia. Tsallis entropy has been shown to be one of the most promising information theoretic methods for quantifying changes in the EEG. In this paper, we develop the approach further. This has yielded an enhanced performance compared to existing approaches.**

I. INTRODUCTION

The number of people living with Alzheimer's disease (AD) and other forms of dementia is rapidly rising and this is creating significant burden on families and on the health and social care systems [1]. Dementia is a set of symptoms caused by damage to the brain. Common symptoms include loss of mental ability, difficulty with finding the right words, changes in personality and mood [2]. AD is the most common cause of dementia, accounting for over 50% of all cases. AD is progressive and in the early stages may present as mild memory loss, but in later stages it can lead to loss of awareness and ability to interact socially. Early diagnosis is widely recognised as important for patients and their families to get maximum benefits from appropriate access to available health and social care and to plan for the future [3].

The EEG (electroencephalogram) can play a useful role as a first line of decision-support tool for early detection and diagnosis of dementia [4]. It is non-invasive, low-cost, has a high temporal resolution and has been shown to contain useful information about brain dynamics in AD [5]. In AD patients, the EEG is characterized by changes in the mean frequency, complexity measures, and in the coherences among cortical regions [6]. These changes in the EEG can be quantified as a biomarker.

A variety of linear and non-linear methods exist for computing biomarkers from the EEG [7]. However, information theoretic methods, entropy-based approaches in particular, have emerged as a potentially useful way to derive robust EEG biomarkers of dementia [8, 9, 10, 11, 12, 13]. They are attractive because of the potential natural link between information theory-based biomarkers and changes in the brain caused by dementia. Changes in the information processing activities caused by damage to nerve cells/pathways in the brain may be reflected in the information content of the EEG and hence in the biomarkers [8].

Tsallis entropy approach has been shown to be one of the most promising information theoretic methods for quantifying changes in the EEG [8, 10, 13]. It has also been shown to be a reliable analysis tool to use with working memory tasks. As its computation is fast, it can serve as a basis for a real-time decision support tool for dementia diagnosis by both specialists and non-specialists. In this paper, we aim to develop it further and to evaluate its performance. This has yielded an enhanced performance compared to existing approaches.

The paper is organised as follows. In Section II, the methodology used in the study is described. In Section III, the materials (including the datasets and EEG recordings) are described. Section IV presents the results and Section V concludes the paper.

II. METHODOLOGY

In our approach, we start by computing the Tsallis entropy for each EEG channel and for each subject from a reference datasets which includes dementia and normal subjects. The entropy values are then normalised to emphasise the differences between the entropy for normal and dementia subjects. The normalised Tsallis entropies are used to create reference feature vectors, one for dementia subjects and one for normal subjects. Subsequently, the feature vector for a new dataset is compared to the reference vectors using K-means clustering to discriminate between AD and normal subjects.

A generalised measure of entropy, due to Tsallis, is given by:

$$S_q = (\sum_{i=1}^{N} P_i - P_i^q)/(q-1) \quad (1)$$

Where S_q is the Tsallis entropy value, N is the number of states that the amplitudes of the EEG are quantized into, P_i is a probability associated with the i^{th} state [14].

The scale range method was used to standardize and normalise the entropy range values as in "(2)". It was found that normalisation is important to prevent clusters that are dominated by the greater values of variation [15].

$$S_{q_i} = \frac{[S_q - \min(S_q)] \times [\max(S_q) - \min(S_q)]}{C} \quad (2)$$

Where S_q is the Tsallis entropy value need to scale, S_{qi} is the scaled value of S_q with i^{th}, $\min(S_q)$ and $\max(S_q)$ represent

the minimum and maximum Tsallis entropy values and C is constant.

III. MATERIALS

Two datasets (Datasets A and B) were obtained from Derriford Hospital. The datasets were collected using normal hospital practices in conjunction with a strict [4]. Dataset A consists of 3 Alzheimer's patients and 8 age-matched controls (over 65 years old) who have normal EEGs. Each case was assessed and confirmed by a consultant clinical neurophysiologist. Dataset B consists of 24 normal subjects and 17 probable AD, which are not perfectly age matched. In normal groups, mean age is 69.4±11.5, minimum 40, maximum is 84, 42% are male. In the AD group, mean age is 77.6±10.0, minimum is 50, maximum is 93, 53% are male.

Dataset A was recorded using the traditional 10-20 system in a Common Reference Montage (by using the average of all channels as the reference) and converted to Common Average and Bipolar Montages in software. Dataset B was recorded using the modified Maudsley system that is similar to the traditional 10-20 system. The Fig. 1 below shows the electrode locations in 10–20 system.

In both datasets, the EEG recordings include various states such as awake, hyperventilation, drowsy and alert, with periods of eyes closed and open. The sampling rate was reduced from 256Hz to 128Hz by averaging two consecutive samples for storage reasons.

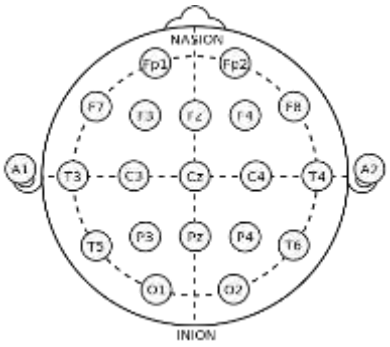

Figure 1. International 10–20 system [16].

IV. RESULTS AND DISCUSSIONS

Following the approach in [4], complete recordings including artefacts were used without a priori selection of elements 'suitable' for analyses. This was to enable us to have an idea about the robustness and usefulness of the method in practice. Data from a fixed interval (61s to 240s) was used to avoid electrical artefacts, which regularly occur at the beginning of a record, therefore give, a standard 3 minutes data to analyse.

EEG analysis to derive the biomarkers was divided into two phases (development Phase, and testing phase) and Tsallis entropy is computed in both phases.

A. Development Phase

In this phase, dataset B was used. We separated the dataset into AD and normal groups. For each group, we computed the Tsallis entropy (Sq) for all 21 channels (N=5120, and q=0.5). Fig. 2 shows the Tsallis entropy for 21 channels to dataset A. Dataset B is used to build the reference feature vectors because it is larger than dataset A and consequently has more diversity.

The scale range method was used to standardize and normalise the data range values. The average values of Tsallis entropy for AD, and normal groups are used to create reference feature vectors which are used in the classification stage.

Fig. 2, Fig. 3, Fig.4, and Fig. 5 illustrate the effects of the scale range normalisation.

B. Testing Phase

Dataset A was used for testing. We computed the average Tsallis entropy as is done in training Phase, and normalise the results. We compared the mean Tsallis entropy values and the reference vectors (computed in the development phase) using k-Means clustering.

We classified a case as AD if the vector was closer the reference vector for the AD group. Otherwise, we classified it as normal. In the study, 15 channels of EEG (F8, A1, T3, C3, CZ, C4, T4, A2, T5, P3, PZ, P4, T6, O1, and O2) are used to detect AD by calculating the normalized value of Tsallias entropy per channel for each individual. We select these channels based on an analysis of the Tsallis values for all channels for normal and dementia subjects.

Fig. 2 shows that Tsallis entropy values for ADs are lower than for the controls. The reduction in Tsallis entropy values is thought to be due to the slowing in the EEG activities as a result of AD and is consistent with the findings in other studies [9].

The performance of our approach was evaluated by calculating sensitivity, specificity, accuracy, precision and f measure. In addition, these measurements were computed based on the True Positive (TP), True Negative (TN), False Negative (FN), False Positive (FP) [17]. The results are summarised in Table 1.

In [13], the overall accuracy was 77%, the sensitivity was 82%, and the specificity was 73% for the counting backward task.

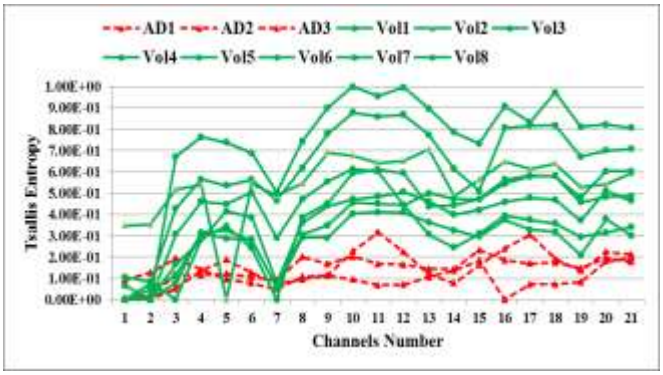

Figure 2. Tsallis entropy for dataset A.

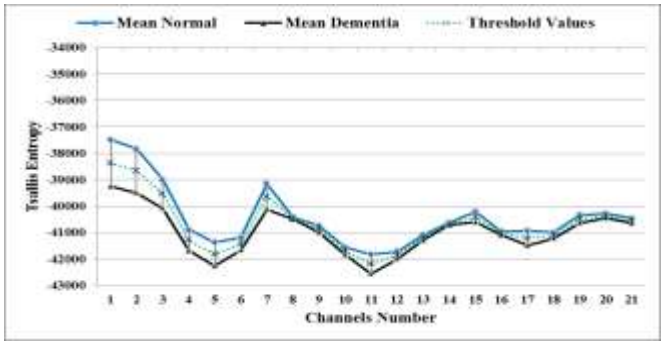

Figure 3. Non-normalized Mean Tsallis for normal and AD - dataset A.

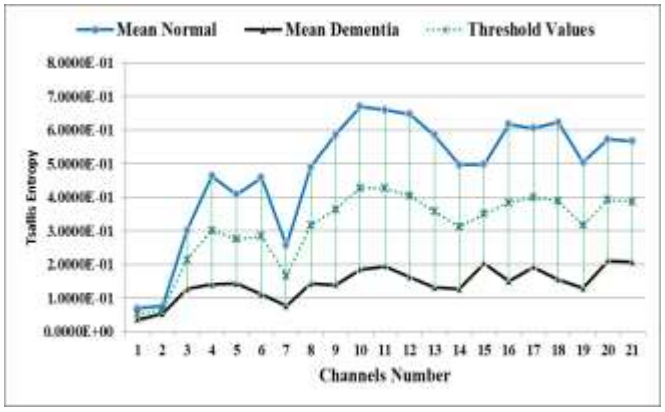

Figure 4. Normalized Mean Tsallis for normal and AD - dataset A.

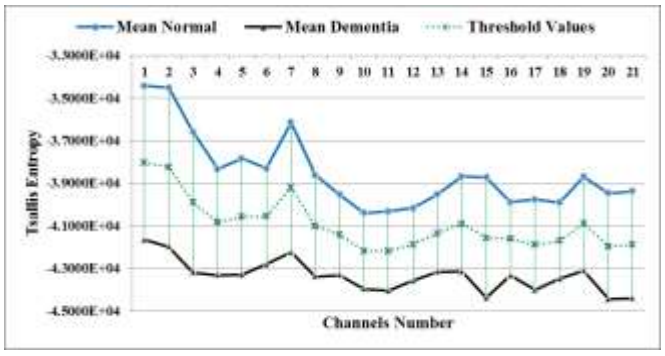

Figure 5. Non-normalized Mean Tsallis for normal and AD-dataset B.

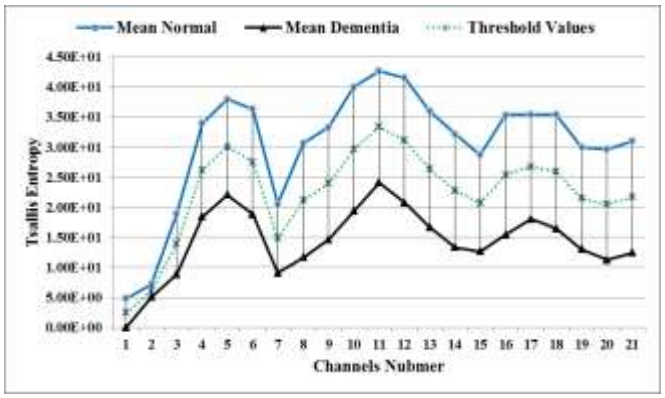

Figure 6. Normalized Mean Tsallis for normal and AD - dataset B.

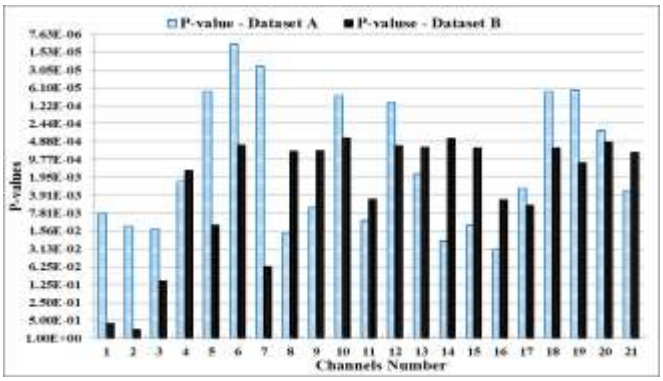

Figure 7. P-values for Tsallis entropy between dataset A and B before normalization.

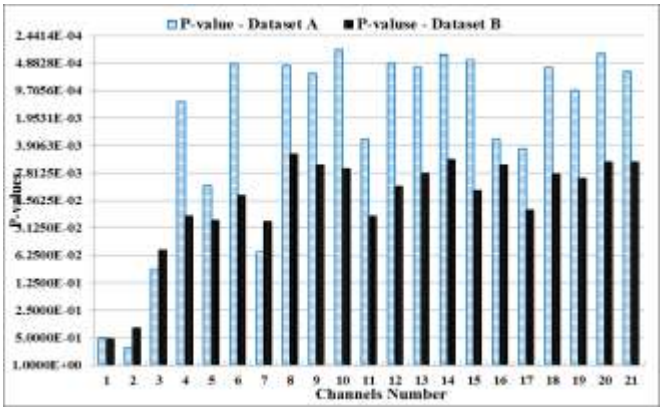

Figure 8. P-values for Tsallis entropy between dataset A and B after normalization.

TABLE I. PERFORMANCE RESULT OF TSALLIS ENTROPY

	Dataset A	Dataset B
Sensitivity	100%	85.7%
Specificity	50%	70.9%
Accuracy	84.6%	78.8%
Precision	72.7%	77.4%
F measure	84.19%	81.33%

V. CONCLUSION

The results suggest that the approach presented here yields enhanced performance for Tsallis entropy-based biomarkers for the detection of dementia. At this level of performance, the approach can serve as a basis for a first line of a decision support tool for detection of dementia. Future work will evaluate the approach more extensively using a larger dataset.

ACKNOWLEDGMENT

The first author would like to thank The Ministry of Higher Education and Scientific Research (MoHESR) - Iraq for their financial support and I thank Dr. Is-Haka Mkwawa, School of Computing and Mathematics, Plymouth

University for his comments.

REFERENCES

[1] M. Prince, M. Guerchet, and E. Albanese “World Alzheimer Report 2014”, September, 2014.

[2] Alzheimer’s Disease Society “What is Dementia?”, Alzheimer’s Disease Society Information Sheet, London, Sep. 2014.

[3] E. C. Ifeachor, N. J. Outram, G. T. Henderson, H. S. K. Wimalaratna, N. Hudson, R. Sneyd, C. Dong, and C. Bigan, “Nonlinear methods for biopattern analysis: role and challenges,” in *Proc. of the 26th Annu. Int. Conf. of the 2004 IEEE EMBS*, pp. 5400–5406.

[4] G. Henderson, E. Ifeachor, N. Hudson, C. Goh, N.Outram, S. Wimalaratna, C. D. Percio, and F. Vecchio. "Development and assessment of methods for detecting dementia using the human electroencephalogram," *IEEE Trans. Biomed. Eng.*, vol. 53, no. 8, pp. 1557–1568, Aug. 2006.

[5] J. Dauwels,F. B. Vialatte, and A. Cichocki, "On the early diagnosis of Alzheimer’s disease from EEG signals: A mini-review," Advances in Cognitive Neurodynamics (II). Springer Netherlands, 2011. pp. 709-716.

[6] C. F. V. Latchoumane, E. Ifeachor, N. Hudson,S. Wimalaratna, and J. Jeong, “Dynamical Nonstationarity Analysis of Resting EEGs in Alzheimer’s Disease,” in *Neural Information Processing*, Springer, Berlin Heidelberg, Jan. 2008, pp. 921-929.

[7] C. Babiloni, G. Binetti, E. Cassetta, G. Dal Forno, C. Del Percio, F. Ferreri, R. Ferri, G. Frisoni, K. Hirata, B. Lanuzza, C. Miniussi, D. V. Moretti, F. Nobili, G. Rodriguez, G. L. Romani , S. Salinari, and P. M. Rossini, “Sources of cortical rhythms change as a function of cognitive impairment in pathological aging: a multicenter study,” *Clin. Neurophysiol.*, vol. 117, no. 2, pp. 252-68, Feb. 2006.

[8] P. Zhao, P. Van-Eetvelt, C. Goh, N. Hudson, S. Wimalaratna, and E. Ifeachor. "Characterization of EEGs in alzheimer's disease using information theoretic methods," in *Engineering in Medicine and Biology Society*, 2007 IEEE EMBS 2007. 29th Annu. Int. Conf. of the IEEE, pp. 5127-5131.

[9] D. Abásolo, R. Hornero, P. Espino, and D. Alvarez, Poza, “Entropy analysis of the EEG background activity in Alzheimer's disease patients,” *J. Physiol. Meas.*, vol. 27, no. 3, pp. 241-53, Mar. 2006.

[10] B. Hamadicharef, , C. Guan, E. C. Ifeachor, N. Hudson, and S. Wimalaratna, "Performance evaluation and fusion of methods for early detection of Alzheimer Disease," in *Int. Conf. on BioMedical Engineering and Informatics 2008 IEEE BMEI*, vol. 1, pp. 347-351.

[11] J. Escudero, D. Abásolo, R. Hornero, P. Espino, and M. López. "Analysis of electroencephalograms in Alzheimer's disease patients with multiscale entropy." *Physiological measurement*, Vol. 27, no. 11, 2006, pp. 1091–1106.

[12] Z. Massimiliano, L. Zunino, O. A. Rosso, and D. Papo, "Permutation entropy and its main biomedical and econophysics applications: a review," *Entropy*, vol 14, no. 8, pp.1553-1577, 2012.

[13] T. D. Bock, S. Das, M. Mohsin, N. B. Munro, L. M. Hively, Y. Jiang, C. D. Smith, D. R. Wekstein, G. A. Jicha, A. Lawson, J. Lianekhammy, E. Walsh, S. Kiser, and C. Black, "Early detection of Alzheimer's disease using nonlinear analysis of EEG via Tsallis entropy," Biomedical Sciences and Engineering Conference 2010 IEEE BSEC, pp. 1-4.

[14] G.-M., Murray and C. Tsallis, *Nonextensive entropy-Interdisciplinary applications.* Oxford University Press, UK, 2004, pp. 79-80.

[15] B. Liu, *Web data mining: exploring hyperlinks, contents, and usage data.* Springer Science & Business Media, 2007, pp.19.

[16] S. Sanei and J. Chambers, *EEG Signal Processing*. John Wiley & Sons, Ltd, 2007, pp.16.

[17] I. H. Witten and E. Frank, Data Mining: Practical machine learning tools and techniques. Morgan Kaufmann, 2005, pp.172.