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Approximate Entropy in the Electroencephalogram During Wake and Sleep

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Abstract

Entropy measurement can discriminate among complex systems, including deterministic, stochastic and composite systems. We evaluated the changes of approximate entropy (ApEn) in signals of the electroencephalogram (EEG) during sleep.

EEG signals were recorded from eight healthy volunteers during nightly sleep. We estimated the values of ApEn in EEG signals in each sleep stage. The ApEn values for EEG signals (mean ± SD) were 0.896 ± 0.264 during eyes-closed waking state, 0.738 ± 0.089 during Stage I, 0.615 ± 0.107 during Stage II, 0.487 ± 0.101 during Stage III, 0.397 ± 0.078 during Stage IV and 0.789 ± 0.182 during REM sleep. The ApEn values were found to differ with statistical significance among the six different stages of consciousness (ANOVA, $p<0.001$). ApEn of EEG was statistically significantly lower during Stage IV and higher during wake and REM sleep.

We conclude that ApEn measurement can be useful to estimate sleep stages and the complexity in brain activity.

Keywords: Electroencephalography, Entropy, Approximate, Nonlinear Analysis, Sleep Stage, System Complexity

INTRODUCTION

The electroencephalogram (EEG) is an important non-invasive measure of the dynamic brain activity. Recently, nonlinear and chaotic theory has been applied to the analysis of EEG signals. The blind application of such methods to actual signals, however, may result in spurious and misleading results.[1]

The approximate entropy (ApEn) was developed by Pincus as a measure of "system complexity".[2,3] A high value of ApEn indicates random and unpredictable variation, whereas a low value of ApEn indicates regularity and predictability in a time series.[2,3] Especially, ApEn can discriminate among a wide variety of systems, including nonlinear deterministic, stochastic and noisy systems, while being applicable to medium-sized time series.[2–5] ApEn has been applied to the analysis of physiological signals. For instance, it was used to recognize epileptic activity.[6] Fell et al[7] reported that the Kolmogorov K2 entropy increased during REM sleep and decreased during slow wave sleep. Since the ApEn can be computed from shorter data series, we here assess any changes in ApEn of EEG signals during eyes-closed wake and five sleep stages (Stage I, Stage II, Stage III, Stage IV and REM sleep) in healthy volunteers.

METHODS

We investigated 8 healthy male volunteers, aged 23 to 26 years (mean ± SD: 24.1±1.1 years). All subjects went to sleep at 11 PM and awoke at 7 AM. Informed written consent was obtained from all subjects.

EEG signals (Synafit 2100, NEC, Tokyo, Japan) were recorded from 10:30 PM to 6:00 AM, while examinees were resting with eyes closed, lying in a darkened, sound-attenuated room. EEG signals were recorded from scalp surface electrodes (F3, F4, C3, C4, O1 and O2 using the International 10–20 System). Surface electrodes were also placed at the outer canthi of both eyes to record eye movements and on the chin to record submental electromyographic activity. Two independent neuroscientists each categorized the stage of consciousness on the EEG records at 30-sec intervals, using the criteria of Rechtschaffen and Kales.[8] We selected five different 10-sec artifact-free epochs from each sleep stage (I, II, III, IV, and REM) for each subject. The C3 EEG position referenced to A2 was chosen to compute ApEn. EEG signals were recorded on a magnetic tape (Instrumentation tape recorder A-47, SONY, Tokyo, Japan), and digitized at a sampling rate of 200-Hz with 12-bit resolution, with high frequency filter of 60-Hz and a time constant of 0.3-sec.

The ApEn of five consecutive artifact-free EEG samples were computed during each sleep stage. In mathematical terms, ApEn is derived from the correlation integral $C_{m,i}(r)$. As described by Pincus,[2,3] the ApEn is computed as:

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

$$\Phi^{m}(r) = (N - (m - 1))^{-1} \sum_{i=1}^{N-(m-1)} \ln C_{m,i}(r)$$

$$ApEn(N, m, r = (N-(m-1))^{-1} \sum_{i=1}^{N-(m-1)} \ln C_{m,i}(r) - (N-m)^{-1} \sum_{i=1}^{N-m} \ln C_{m+1,i}(r).$$

ApEn involves the following parameters: the vector length m, the "filter factor" r, and the number of data points N. The value of N for the ApEn computation is typically between 75 and 5000.[2,3] ApEn measures the logarithmic likelihood that sets of patterns that are close for m-observations remain close on the next incremental comparisons.[2,3] ApEn characterizes how different segments of the signal with similar recent histories remain similar in the future. Insofar as ApEn decreases, the complexity of the signal is low and determinism is high.

In this study, the number of data (N) is 2000 (10-sec). We set the "filter factor" r to be 0.2 times the standard deviation of the original data series, and used length 2 (m = 2).[2–5] In order to facilitate the interpretation of ApEn values of EEG signals, the ApEn of a sine wave was estimated to be 0.0001 (N = 2000) as an example of a regular (linear) signal. The ApEn values of the Lorenz[9] and Rössler[10] models of chaotic signals were estimated to be 0.135 and 0.218, respectively (N = 2000). The ApEn of a series of uniformly distributed random numbers was estimated to be 1.909 (N = 2000). We used the MatLab software (MathWorks, Inc., Natick, MA, USA) to compute the ApEn values.

Statistical analyses

The values of ApEn are presented as means ± SD. We used two-way analyses of variance (ANOVA) for the assessment of any difference among sleep stages. Scheffe's test (StatFlex, ViewFlex, Tokyo, Japan) was used when multiple comparisons were performed. Differences were considered to be statistically significant at $P < 0.05$.

RESULTS

The ApEn values of EEG signals were 0.896 ± 0.264 during eyes-closed wake, 0.738 ± 0.089 during Stage I, 0.615 ± 0.107 during Stage II, 0.487 ± 0.101 during Stage III, 0.397 ± 0.078 during Stage IV and 0.789 ± 0.182 during REM sleep, (Figure 1). The ApEn values were found to differ with statistical significance among the six different stages of consciousness (ANOVA, $p<0.001$) (Figure 1). The ApEn was statistically significantly higher during eyes-closed wake than during Stage II ($p<0.01$), Stage III ($p<0.001$) and Stage IV ($p<0.001$). The ApEn was statistically significantly lower during Stage IV sleep than during Stage I ($p<0.01$) or REM sleep ($p<0.001$). The ApEn was also statistically significantly lower during Stage III sleep than during Stage I sleep ($p<0.05$) or REM sleep ($p<0.01$). The intra-subject coefficients of variation of the ApEn values during each stage were 8.3 ± 4.1% (Stage I), 10.6 ± 3.4% (Stage II), 15.4 ± 4.4% (Stage III), 15.0 ± 5.5% (Stage IV), and 9.9 ± 6.7% (REM).

Figure 1

ApEn in EEG signals during eyes-closed wake and different sleep stages in 8 healthy subjects (mean ± SD, ANOVA, $p < 0.001$).

In order to eliminate the inter-individual variation, the data from each subject were expressed as a percentage of the mean ApEn value computed for that subject across the six different stages of consciousness. The percentage change of ApEn in EEG during each stage was then obtained by subtracting 100%, (Figure 2). The ApEn is seen to be invariably below average during Stages III and IV sleep, while it is invariably above average during REM sleep and eyes-closed wake condition. The percentage change in ApEn was found to differ with statistical significance among the six different stages of consciousness (ANOVA; $p<0.001$). The percentage change of ApEn during each stage was 34.8 ± 20.8% during eyes-closed wake, 14.3 ± 11.3% during Stage I, −4.4 ± 19.0% during Stage II, −24.3 ± 4.4% during Stage III, −41.0 ± 8.4% during Stage IV and 20.1 ± 17.4% during REM sleep, (Figure 2).

Figure 2

Percentage change in mean ApEn value for each healthy subject during different stages of consciousness (n=8, ANOVA; $p<0.001$).

DISCUSSION

As a measure of entropy, ApEn can be computed using short and noisy experimental data sets, irrespective of the presence of any nonlinear properties. In this study, we found statistically significant changes in ApEn during different stages of consciousness in healthy subjects, with lowest values during Stage IV and highest values during REM sleep (Figure 1). Among all states, ApEn was highest during eyes-closed wake. These results, in keeping with those of Fell et al[7] based on the Kolmogorov K2 entropy, suggest that complexity in the brain increases during waking and REM stage, and decreases in slow wave sleep. Moreover, the differences among all stages were more clearly apparent for the ApEn than for the K2 measure of entropy. ApEn could be used to identify changes in consciousness.

System complexity has recently been analyzed in EEG signals using several new methods of nonlinear analysis. In particular, the correlation dimension (D2)[11] has been used to estimate the complexity and nonlinearity of EEG signals.[12,13] D2 in EEG records during sleep, calculated according to the algorithm of Grassberger and Procaccia,[11] has been shown to assume statistically significantly different values during different sleep stages. When sleep deepens, D2 decreases, but D2 is larger during rapid eye movement (REM) sleep,[14] a result corroborated herein on the basis of the ApEn.

Although previous studies in which D2 was used suggested that resting EEG signals in healthy subjects had chaotic dynamics and nonlinear properties,[14] others concluded that EEG signals could not be distinguished from a Gaussian linear stochastic process. The controversy stems in part from the difficulty in computing D2 for EEG signals that are both non-stationary and high-dimensional.[15] Usually, the validity of D2 is tested by surrogate data analysis.[15–18] Entropy measurement can also estimate complex systems, including nonlinear deterministic and stochastic signals.[2] From this viewpoint, the ApEn measurement may be useful to analyze EEG data.

The inter-subject variability of ApEn, illustrated in Figure 2 for the average percentage change in ApEn across all stages of consciousness, is particularly large during eyes-closed wake, Stage I and Stage II sleep. This may be related to the variable brain conditions during the waking state. In addition, the change in ApEn value seen during the transition from waking to light sleep may also be associated with an increase in inter-subject variability during Stage I sleep. The occurrence of K-complexes and spindles may further increase the variability of ApEn during stage II sleep (Figure 2). The smaller inter-subject variability observed during Stages III and IV sleep may relate to the decreased brain complexity in slow wave sleep. It has been recently suggested that the ApEn is useful to measure the extent of regularity in EEG signals during anesthesia, when ApEn values are reportedly decreased.[19] ApEn of EEG signals may be clinically useful by providing a more rigorous estimate of sleep stages.

Although the analyses in this study are presented for only one electrode site and one reference, it is well known that EEG signals from different electrode pairs provide important and useful information.[20] Previous reports revealed that the topographical distribution of Kolmogorov K2 entropy from different electrode pairs was useful to detect EEG changes during affective induction.[21] The values of ApEn from multiple electrodes in EEG may give more information about brain dynamics.

In conclusion, ApEn could serve to estimate sleep stages in EEG signals, complementing other approaches based on spectral aspects of the action potentials of the brain in health and disease states.[22] Moreover, the ApEn can be computed using short experimental data sets despite the lack of nonlinear properties. ApEn measurement in EEG may be clinically useful to estimate sleep stages and quantify brain activity. Further study is needed to clarify the usefulness of the ApEn in relation to the automatic diagnosis of sleep stages.

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References

1. Schreiber T. Interdisciplinary application of nonlinear time series methods. *Physics Reports.* 1999;308:1–64. [Google Scholar]

2. Pincus SM. Approximate entropy as a measure of system complexity. *Proc Natl Acad Sci USA.* 1991;88:2297–2301. [PMC free article] [PubMed] [Google Scholar]

3. Pincus SM. Irregularity and asynchrony in biologic network signals. *Methods Enzymol.* 2000;321:149–182. [PubMed] [Google Scholar]

4. Kaplan DT, Furman MI, Pincus SM. Aging and the complexity of cardiovascular dynamics. *Biophys J.* 1991;59:945–949. [PMC free article] [PubMed] [Google Scholar]

5. Burioka N, Cornélissen G, Halberg F, Kaplan DT, Suyama H, Sako T, Shimizu E. Approximate entropy of human respiratory movement during eye-closed wake and different sleep stages. *Chest.* 2003;123:80–86. [PubMed] [Google Scholar]

6. Diambra L, de Figueiredo JCB, Malta CP. Epileptic activity recognition in EEG recording. *Physica A.* 1999;273:495–505. [Google Scholar]

7. Fell J, Röschke J, Mann K, Schäffner C. Discrimination of sleep stages: a comparison between spectral and nonlinear EEG measures. *Electroencephalogr Clin Neurophysiol.* 1996;98:401–410. [PubMed] [Google Scholar]

8. Rechtschaffen A, Kales A. *BIS/BRI.* Los Angeles: University of California; 1968. A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. [PubMed] [Google Scholar]

9. Lorenz EN. Deterministic nonperiodic flow. *J Atmos Sci.* 1964;20:130–141. [Google Scholar]

10. Rössler DE. An equation for continuous chaos. *Phys Lett.* 1976;57A:397–398. [Google Scholar]

11. Grassberger P, Procaccia I. Characterization of strange attractors. *Phys Rev Lett.* 1983;50:346–349. [Google Scholar]

12. Pritchard WS, Duke DW, Krieble KK. Dimensional analysis of resting human EEG II. Surrogate data testing indicates nonlinearity but not low-dimensional chaos. *Psychophysiology.* 1995;32:486–491. [PubMed] [Google Scholar]

13. Kobayashi T, Madokoro S, Wada Y, Misaki K, Nakagawa H. Human sleep EEG analysis using the correlation dimension. *Clin Electroencephalogr.* 2001;32:112–118. [PubMed] [Google Scholar]

14. Röschke J, Aldenhoff J. A nonlinear approach to brain function: deterministic chaos and sleep EEG. *Sleep.* 1992;15:95–101. [PubMed] [Google Scholar]

15. Theiler J, Rapp PE. Re-examination of the evidence for low-dimensional, nonlinear structure in the human electroencephalogram. *Electroencephalogr Clin Neurophysol.* 1996;98:213–222. [PubMed] [Google Scholar]

16. Burioka N, Cornélissen G, Halberg F, Kaplan DT. Relationship between correlation dimension and indices of linear analysis in both respiratory movement and electroencephalogram. *Clin Neurophysiol.* 2001;112:1147–1153. [PubMed] [Google Scholar]

17. Theiler J, Eubank S, Longtin A, Galdrikian B, Farmer JD. Testing for nonlinearity in time series: the method of surrogate data. *Physica D.* 1992;58:77–94. [Google Scholar]

18. Miyata M, Burioka N, Sako T, Suyama H, Fukuoka Y, Tomita K, Higami S, Shimizu E. A short daytime test using correlation dimension for respiratory movement in OSAHS. *Eur Respir J.* 2004;23:885–890. [PubMed] [Google Scholar]

19. Bruhn J, Bouillon TW, Radulescu L, Hoeft A, Bertaccini E, Shafer SL. Correlation of approximate entropy, bispectral index, and spectral edge frequency 95 (SEF95) with clinical signs of "anesthetic depth" during coadministration of propofol and remifentanil. *Anesthesiology.* 2003;98:621–627. [PubMed] [Google Scholar]

20. Nunez PL. Toward a quantitative description of large-scale neocortical dynamic function and EEG. *Behav Brain Sci.* 2000;23:371–398. [PubMed] [Google Scholar]

21. Aftanas LI, Lotova NV, Koshkarov VI, Pokrovskaja VL, Popov SA, Makhnev VP. Non-linear analysis of emotion EEG: calculation of Kolmogorov entropy and the principal Lyapunov exponent. *Neurosci Lett.* 1997;226:13–16. [PubMed] [Google Scholar]

22. Halberg F, Cornélissen G, Bingham C, Witte H, Ribary U, Hesse W, et al. Chronomics: imaging in time by phase synchronization reveals wide spectral biospheric resonances beyond short rhythms. *Neuroendocrinol Lett.* 2003;24:355–380. [PubMed] [Google Scholar]