DYNAMICAL NONSTATIONARITY OF THE EEG IN PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (AD/HD) DURING COGNITIVE TASKS

Charles-Francois V. Latchoumane,* In-Hye Kim,**
Doheon Lee,* Kwang H. Lee,* Jaeseung Jeong*

* Department of BioSystems,
Korea Advanced Institute of Science and Technology (KAIST),
Daejeon, South Korea 305-701
**Department of Physics
Kongju National University
Kongju, South Korea 314-701

jsjeong@kaist.ac.kr

Abstract: Time series generated from nonlinear dynamical systems can exhibit statistical nonstationarity, despite that their parameters in the dynamical process remain all constant. In other words, dynamical stationarity of the time series does not indicate its statistical stationarity. The aim of this study is to investigate the dynamical nonstationarity of the EEG in patients with Attention-Deficit/Hyperactivity Disorder (AD/HD) during cognitive tasks. We hypothesize that AD/HD patients have difficulties in maintaining a specific cognitive state and thus their EEGs exhibit highly frequent dynamical changes. To test this hypothesis, we recorded EEGs from 16 adolescent subjects with AD/HD and 18 age-matched healthy subjects in a resting state and during cognitive tasks, and estimated the mean duration of the dynamically stationary states for both groups. We found that the AD/HD patients had a significantly shorter duration of dynamically stationary states than those of controls. This result indicates that AD/HD patients exhibit more frequent dynamical changes in the brain than controls, which might reflect the more frequent cognitive-state transition in the AD/HD brain. This finding suggests that dynamical nonstationarity of the EEG is a useful tool for diagnosis of AD/HD.

Introduction

Attention-Deficit/Hyperactivity Disorder (AD/HD) is a common behavioral disorder which is characterized by inattention, hyperactivity, impulsivity, and aggressiveness. AD/HD affects 4-7% of school children and 2-3% of adults, resulting in troubles in school, familial, and social life. Although there are lots of studies reporting the morphological and functional abnormalities in AD/HD patients, the pathogenesis of the disease is still not clear. Furthermore, because there is no definite diagnostic tool for determining the presence of the disease, the diagnosis of AD/HD primarily depend on questionnaires and psychological evaluations.

There have been some EEG studies on AD/HD patients using Fourier transformation analysis such as discriminant function analysis (2) and absolute/relative power ratio analysis (3) to find that linear analysis of the EEG can classify the AD/HD (and possibly its subtypes) and normal controls with accuracy of 80% (4).

Recently, nonlinear dynamical methods appear to be a promising tool for investigating brain dynamics. The application of these methods to EEG in patients with the neurological and psychiatric disorders has proved an effective and reliable means to diagnose various brain diseases and to quantify the progress of the diseases (for review, Jeong, 2004; Stam, 2005).

In this talk, we introduce the concept of dynamical nonstationarity of the time series to examine the dynamical change in EEG recordings. Time series generated from nonlinear dynamical systems exhibit nonstationary (i.e. time-dependent) based on statistical measures including the mean and variance, despite that their parameters in the dynamical process remain all constant. It indicates that statistical stationarity of the time series does not indicate its dynamical stationarity. Given that the EEG is possibly gnenerated by the dynamical, cognitive process of the brain, dynamical nonstationarity of the EEG can reflect on state transition of the brain. In this assumption, Le Van Quyen et al. (2001) and Dikanev et al. (2005) have applied this method to investigate the possibility of seizure prediction using EEGs in epileptic patients (5, 6).

The aim of this study was to examine the characteristic time length of dynamically stationary EEG epochs in AD/HD patients in a resting state and during cognitive tasks. We hypothesize that AD/HD patients have difficulties in paying attention to one thing for long and therefore they possibly exhibit more frequent dynamical changes in EEGs than normal controls, which implies more frequent dynamical changes in AD/HD brains. To test this hypothesis, we recorded EEGs in 16 channels from 16 adolescent patients with AD/HD and 18 age-matched normal

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subjects in a resting state (5 mins.) and during cognitive tasks (10 mins.), and estimated to compare the characteristic time length, which is defined as the mean duration of a dynamically stationary EEG epoch, in both groups. Short characteristic time length indicates more freqeuent occurrence of dynamical changes in EEGs. We also compared the properties of dynamical stationarity with those of statistical stationarity in EEGs.

Materials and Methods

Dynamical and Statistical nonstationarity analysis

The importance of the dynamical nonstationarity analysis is to identify the dynamical structure of the data, instead of the commonly used statistical one. Several methods to detect dynamical changes between two or within intervals of time series, including recurrence plot (8), statistical test on the reconstructed phase space (9), recurrence time statistics (10), space time index plot (11), nonlinear cross prediction (12), and attractor density distribution (13). In this study, we used attractor density distribution method having relatively low computational expense and sensibility in detecting even slight dynamical changes, compared with other methods.

Distance of Attractor density: This method is based on comparison of the density of the attractor between two successive intervals within the time series (13). The Phase space reconstruction provides a multi-dimensional topology of the underlying dynamics of the system. A bundle of trajectories in the reconstructed phase space is called the attractor, which implicates dynamics underlying the time series.

Let the x(i) be the ith value of the given time series X, and i be an integer indexing the time position of the time series x(i). First, we normalized the data into S bins and compared several intervals under the same conditions, explained as follows:

$$0 \le S(x(i)) = Floor\left[\frac{S*(x(i)-x_{\min})}{(x_{\max}-x_{\min})}\right] \le S-1 \qquad (1)$$

In eq. 1, x_{min} and x_{max} are the minimum and maximum value of two successive intervals to be compared, respectively. S is an integer parameter, and the Floor is a function which returns the next lower integer of its input. It requires that $S(x_{max}) = S-1$. From the normalized and binned time series s(i)=S(x(i)), we proceeded on a phase space reconstruction using delay coordinate according to the Takens' theorem (14), as described in eq. 2:

$$V_i=\{s(i),s(i+\tau),...,s(i+(d-1)*\tau)\},i=1...N-(d-1)*\tau \qquad (2)$$

$\mathbf{V_i}$ is a d-dimensional vector, and N indicates the total number of points in the interval. d and τ are the embedding dimension and time delay, respectively, which are important phase-space reconstruction parameters under the constrain $\tau \geq 1$. The values of the parameters S, τ and d were determined empirically based on both sensibility to dynamical changes and low computation consumption, and kept constant for all analyses. The following step was to consider our partitioned the phase space, and summed the population of point in each bin or hypercubes, and estimated the frequency occupation distribution function. We assigned an identification number, I_i to each vector $\mathbf{V_i}$, depending on its unique base S arithmetic writing converted into base 10 as follow:

$$I_i = \sum_{i=1}^{d} V_i(k) * S^{k-1} \qquad (3)$$

Thus, each bin has a unique identification number, easy to link to a vector $\mathbf{V_i}$. The number $\mathbf{V_i}(k)$ in eq. 3 is the kth component of the vector $\mathbf{V_i}$ which is equal to or larger than 0 and lower than S-1. For the evaluation of the distance between two intervals, we used the well suited χ^2 to compare distribution functions:

$$\chi^2(Q,R) = \sum_{i=1}^{L} \frac{(Q_i - R_i)^2}{Q_i + R_i}, \qquad (4)$$

where L is the same total number of bin of the distributions Q and R which are called base and test case distributions, respectively. Finally, we normalized outputs dividing by 2*L, which is the theoretical maximum value taken by χ^2.

Statistical analysis: To investigate the usefulness of the dynamical stationarity, we first should compare it with conventional weak statistical stationarity based on the mean and the variance of the segments in EEGs.

Distribution of the quasi-stationary time interval: The EEGs were divided into L non-overlapping segments. Dynamical and statistical stationarity were examined within the interval and its consecutive one. The statistical outputs were used taking the absolute value of the difference normalized by the respective maximum value. For such relative comparisons of the interval, it is useful to introduce in a significance deviation value σ to enhance the contrast between outcomes (17), given in equation 7:

$$\sigma(i) = \frac{x(i) - \mu}{\delta} \qquad (5)$$

Where, μ and δ are the mean and standard deviation of the EEG under study. We defined a crossing threshold signal as the change of dynamical state, defined by: P[σ, k] ≤ p, where P is the Chi-square cumulative distribution function with k degree of liberty at the value of significance deviation σ. The crossing threshold signal indicates a percentage of the standard deviation above the mean of the interval. Dynamics transition points were used as flags to calculate inter-quasi-stationary intervals, and thus we obtained the distribution of the quasi-stationary time interval for the EEG. The different techniques used for the analysis allow us to observe a distribution of stationary time lengths for each channel of the EEG for each subject. The distribution of the channels of the weighted average of the stationarity time length distribution was calculated. The weighted Average is simply computed as follows in eq. 6:

$$C_i = \frac{\sum_j f_{i,j} * j}{\sum_j f_{i,j}} \qquad (6)$$

Where C_i is the channel considered, and $f_{i,j}$ the frequency of the time length j of the channel C_i, and j a integer belonging to [0,FT] and a value of the time length, FT the maximum time length found in the system. The each time length and average time length was obtained by multiplying j by the number of points considered for an interval L, then divided by the sampling frequency(250 Hz).

Parameters estimation: We partitioned the EEG in 5 seconds (L = 1,250 points) non-overlapping intervals. The use of non-overlapping intervals have the estimated values highly depend on the number of point L: too few points might render the reconstruction obsolete, and too many points can hide short variations. The embedding dimension d and the time delay τ for the phase space reconstruction (eq. 2) were deduced from previous studies (8, 13, and 15), i.e. the first minimum of the mutual information for determination of τ (15). We found d = 5 and τ =30 to be good values to produce reliable results considering topology reconstruction of the attractor and the small number of points of intervals. We used S = 14 ±5 for the density attractor analysis (13); this variable defines the size of the neighborhood in attractor analysis. We used the values k = 7 for the Chi-square cumulative distribution function degree of liberty, and deduced p = 0.02 (Chebyshev's inequality) for the p-value or threshold, and 0.32 was used as the crossing threshold signal.

EEG recordings: EEGs were recorded in 16 channels from 16 adolescent subjects diagnosed as AD/HD by by DSM IV and 18 age-matched healthy subjects in a resting state with eyes-closed and eyes-opened during auditory and visual tasks (1.5 minutes per each). EEG signals were sampled at 250Hz, and 60 Hz and 0.1-125 Hz band-pass filters were used to reduce noise. Simulations were performed using MATLAB 7.0.4 on a 1.6 GHz Pentium 4 computer platform.

Results

We estimated the average of time length on each electrode in AD/HD patients and normal subjects as shown in Figure 1 and 2. Figure 1 shows that AD/HD patients have shorter time length of dynamical stationary EEG than controls, particularly at channel C3, C4 (central), P3, P4 (parietal) and O1, O2 (occipital), in a resting state with eyes closed and during the auditory task. The mean value of the time for both states was not higher than 2.6 index of time (i.e. 13 seconds). This result indicate that AD/HD patients exhibit more frequent occurrence of dynamical changes in EEGs and thus higher degree of dynamical nonstationarity than healthy subjects.

AD/HD patients have shorter mean duration of statistical stationary EEGs than normal controls, particularly in F1-F8 region (frontal), as shown in Figure 2 (a). However, Figure 2 (B) does not exhibit distinction between two groups. Furthermore, the mean values of the time for Fig. 2(A) and 2(B) were higher than 5 index of time (i.e. 25 seconds).

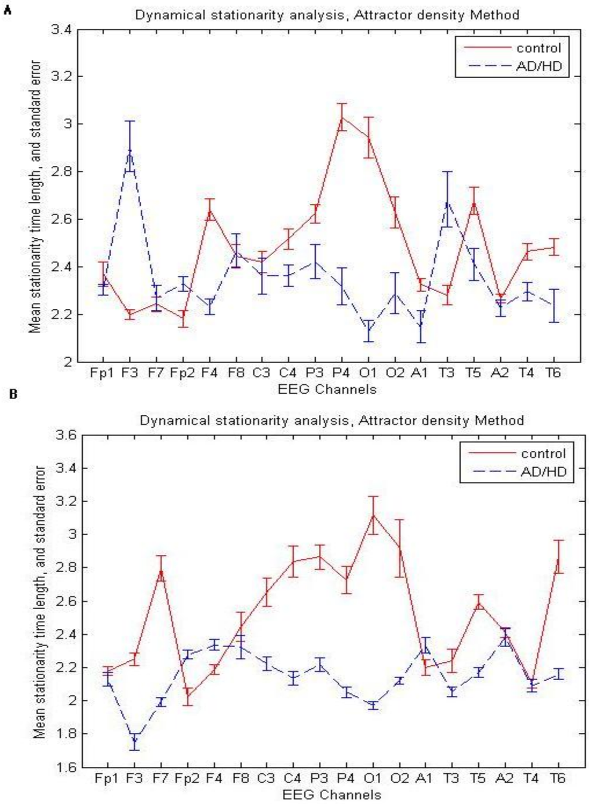

Figure 1: Mean of dynamical stationarity time length of control and AD/HD subjects, for resting Eyes closed (A) and Auditory task (B) state, over all EEG channels. Interval number of point is 1250 (5 seconds), d = 5, τ =30, k = 7.

Discussion

In this study, we found that AD/HD patients have shorter characteristic time length of dynamical stationary EEGs than healthy normal controls during auditory task. This finding suggests that the degree of dynamical nonstationarity can be a good measure for quantifying the frequency of occurrence of dynamical changes in EEG which reflect state transition of the brain. Abnormally frequent state transition of the brain in AD/HD results in high degree of dynamical nonstationarity. We suggest that this measure might be a good tool for diagnosing and quantifying AD/HD. This finding implicates some association between dynamical changes in EEGs and the state transition of the brain. More specifically, in AD/HD case, the attention and hyperactivity symptoms should be closely related to instability in the stationary dynamics of the brain. Therefore, the stationarity should exhibit the shorter time length than normal controls. We should note that, in almost all cases, statistical stationary segments are longer than dynamical one, and the statistical stationarity clearly do not imply the dynamical one.

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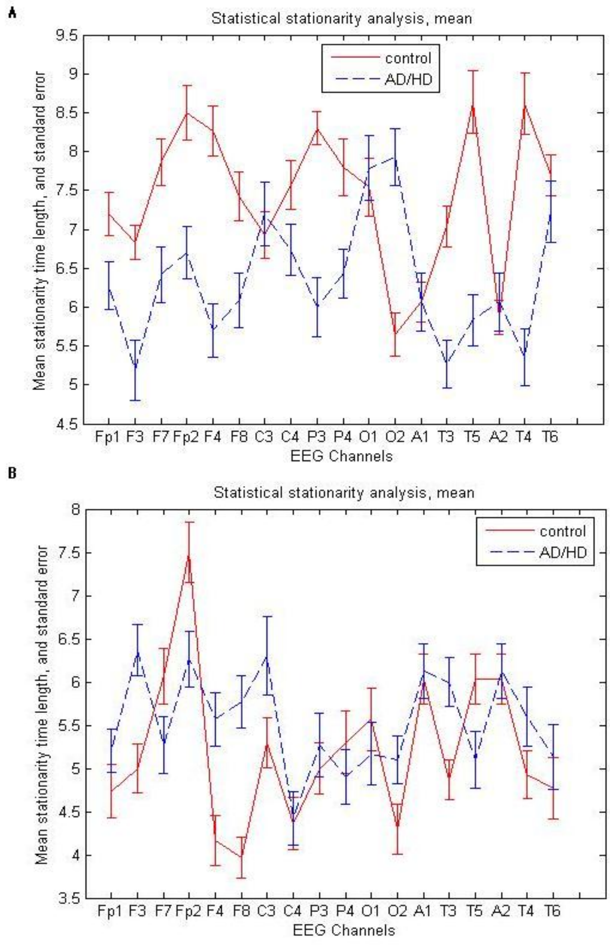

Figure 2: Mean of statistically stationarity time length of control and AD/HD subjects in a resting condition with eyes closed (A) and during auditory task (B) over all EEG channels. The number of data points in an interval is 1,250 (5 seconds) with $d = 5$, $\tau = 30$, $k = 7$.

For future work, we should increase the number of subjects and the duration of the resting and cognitive tasks, to obtain a better statistical estimation of the two populations. Furthermore, since AD/HD is a very heterogeneous disease, it is very critical to differentiate subtypes and related disorders using this method. We also work on associating more dynamical and statistical stationarity tests to the study, since they are not all totally equivalent. However, some of these tests (10, 11, and 12) require far more points for the phase space reconstruction (20 seconds intervals at 250 Hz sampling frequency) to keep their interpretability, which would lead us to the use of sliding and overlapping intervals method, also benefic for presented methods. The phase space reconstruction scheme could also switch with one more privileged by biologist for physiological data, the threshold-crossing interspike interval (17).

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References

[1] ROBERT J. BARRY, ADAM R. CLARKE, AND STUART J. JOHNSTONE (2003): 'A review of electrophysiology in attention-deficit/hyperactivity disorder: I. Qualitative and Quantitative electroencephalography,' *Clinical Neurophysiology*, *Elsevier* 114, pp. 171-183

[2] C. MANN, J. LUBAR, A. ZIMMERMAN, C. MILLER, AND R. MUENCHEN (1992): 'Quantitative analysis of EEG in boys with attention-deficit/hyperactivity disorder: controlled study with clinical implications,' *Pediatr. Neurol.*, 8, pp.30-36

[3] V. MONASTRA, J. LUBAR, AND M. LINDEN (2001): 'The development of a quantitative electroencephalographic scanner process for attention-deficit/hyperactivity disorder: reliability and validity studies," *Neuropsychology*, 15, pp.136-144

[4] R. CHABOT, AND G. SERFONTEIN (1996): 'Quantitative electroencephalographic profiles of children with attention-deficit/hyperactivity disorder,' *Biol. Psychiatry*, 40, pp. 951-963

[5] M. LE VAN QUYEN, J. MARTINERIE, V. NAVARRO, P. BOON, M. D'HAVE, C. ADAM, B. RENAULT, F. VARELA, AND M. BAULAC (2001): 'Anticipation of seizures from standard EEG recordings,' *The Lancet*, VOL. 357, pp. 183-188

[6] T. DIKANEV, D. SMIRNOV, R. WENNBERG, J.L. PEREZ VELAZQUEZ, AND B. BEZRUCHKO (2005): 'EEG nonstationarity during intracranially recorded seizures: Statistical and dynamical analysis,' *Clinical Neurophysiology*, *Elsevier*, pp. 1-12

[7] J. BIEDERMAN, S.V. FARAONE, T. SPENCER, T. WILENS, D. NORMAN, K.A. LAPEY, E. MICK, B.K. LEHMAN AND A. DOYLE (1993): 'Patterns of psychiatric comorbidity, cognition, and psychosocial functioning in adults with attention deficit hyperactivity disorder,' *American Psychiatric Association*, 150, pp. 1792-1798

[8] J.-P. ECKMANN, S. KAMPHORST, AND D. RUELLE (1997): 'Recurrence plots of dynamical systems,' *Europhys. Lett.*, 4, pp. 973-977

[9] M. B. KENNEL (1996): 'Statistical test for dynamical nonstationarity in observed time series data,' *Physical Review E*, VOL. 56, No 1

[10] J.B. GAO (2001): 'detecting non stationarity and state transitions in time series,' *Physical review E*, VOL. 63

[11] DEJIN YU, WEIPING LU, AND ROBERT G. HARRISON (1998): 'Detecting dynamical nonstationarity in time series data,' *American Institute of Physics*, VOL. 9, No 4

[12] THOMAS SCHREIBER (1997): 'Detecting and Analyzing Nonstationarity in a time series using nonlinear cross prediction,' *Physical Review Letter*, VOL. 78, No 5

[13] L.M. HIVELY, P.C. GAILEY, V.A. PROTOPOPESCU (1999): 'Detecting dynamical change in nonlinear time series,' *Physical Letters*, *Elsevier*, A258, pp. 103-114

[14] F. TAKENS (1980): "Detecting strange attractors in turbulence," in Dynamical Systems and Turbulence, (Ed): D. rand and L.-S. Young (Springer, Berlin 1980), pp. 336-381

[15] J. S. IWANSKI, AND E. BRADLEY (1998): 'Recurrence plots of experimental data: to embed or not to embed,' *American Institute of Physics*

[16] THOMAS SCHREIBER (1998): "Interdisciplinary application of nonlinear time series methods,' *archXiv: Chaos-dyn/9807001*, v1 pp. 1-86

[17] N. B. JANSON, A. N. PAVLOV, A. B. NEIMAN, AND V. S. ANISHCHENKO (1998): 'Reconstruction of dynamical and geometrical properties of chaotic attractors from threshold-crossing interspike intervals,' *The American Physical Society*, VOL. 58, No. 1

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