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Comparing Developmental Changes of Hippocampal EEG During REM Sleep Using Correlation Dimension

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Abstract. This paper presents a nonlinear dynamics analysis of the ontogeny of the hippocampal EEG recorded from electrodes implanted at two primary sites that generate the theta rhythm—the pyramidal cell layer at CA1 and the granule cell layer at the dentate gyrus. The hippocampal EEG was collected during the vigilance state of REM sleep from freely moving rats of 15 and 90 days of age. The correlation dimension of EEG was estimated using a modified Grassberger-Procaccia method where the correlation integral was computed via a normalized Euclidean distance and proven less sensitive to the embedding dimension. It was observed in the current study that the estimated correlation dimension measures of the REM sleep EEG recorded from the dentate gyrus are significantly larger than those of CA1 in rats of 15 day of age, whereas the difference diminishes as rats mature at 90 days of age. This finding adds a new interpretation from the nonlinear dynamics perspective to compare the developmental differences between the granule cells at the dentate gyrus and the pyramidal cells at CA1 when the theta activity was present during REM sleep.

Keywords: Hippocampal EEG; REM Sleep; Nonlinear Dynamics; Chaos; Correlation Dimension;

1. Introduction

Hippocampal subfields CA1 and the dentate gyrus are known as two primary generators of the hippocampal EEG pattern known as theta (θ) rhythm [Bland et al.,1975; Leung, 1984]. Theta activity first appears in rats at 10 - 12 days of age and matures during the pre-weaning period of development. This electrographic event appears to gradually change its frequency characteristics as the animal matures in our previous studies conducted on the ontogeny of the hippocampal EEG [Bronzino et al., 1976; Ning and Bronzino, 1990, 1993, 1998].

In rats, the pyramidal cells of region CA1 are in place at the time of birth, while about 20% of the adult granule cells are present in the dentate gyrus. Nearly 80% of the granule cells found in the adult dentate arises during the first three weeks of postnatal development [Bland et al.,1975]. The differential development of these two principal cell populations makes it important to examine the time-frame within which local-circuit neurons begin to modulate cellular excitability in both CA1 and the dentate gyrus [Leung, 1984; Bronzino et al.,1976].

For years the hippocampal EEG has been extensively studied through various signal processing methods [Leung, 1984; Bronzino, 1984; Ning and Bronzino, 1990, 1993, 1998]. For instance, studies using the power spectrum have revealed that the peak theta frequency initially around 4-5 Hz at birth shifts to 7-8 Hz by 30 days of age [Bronzino, 1976]. However, the fundamental assumption of linear model based signal analysis tools excludes the possibility of observing any nonlinear behavior hidden within data measurements. And, nonlinear model based signal processing approaches, on the other hand, have added new interpretation with regard to the composition of the EEG [Ning and Bronzino, 1993,1998]. For instance, bispectral analyses were employed to quantify the developmental changes of the hippocampal EEG at subfields of region CA1 and the dentate gyrus. In particular, evidence has demonstrated the existence of quadratic phase coupling (QPC) in the EEG collected from CA1 and the dentate gyrus during REM sleep; the bicoherence function—a measure describing the significance level of QPC—also has been utilized as a quantitative index to delineate the developmental changes in the hippocampal formation of CA1 and the dentate gyrus [Ning and Bronzino, 1993,1998].

Nonlinear and chaotic signal analysis techniques [Hilborn, 2000; Strogatz, 2001; Gao et al., 2007] have emerged more recently and have gained popularity in research because of its unique ability to capture valuable information that other traditional analysis tools fail to provide. In addition, the development of computationally efficient algorithms and fast computing facility significantly alleviate the concern of heavy computation; and emerging proven application examples too help push nonlinear and chaotic analysis for better acceptance in the research arena. In theory, nonlinear and chaotic behaviors naturally appear in a wide variety of physical signals, including biological events; and nonlinear dynamics studies open a door to new theoretical and conceptual interpretations that can further our understanding of the complex systems of interest. Application examples of nonlinear dynamics and chaos are abundant in the literature [Strogatz, 2001; Gao et al., 2007; Takens, 1981; Fell et al., 2001; Pritchard and Duke, 1995; Ning and Wei, 2008; Ning et al., 2009], to name a few. Though the nonlinear and chaotic analysis tools are equipped with unique signal processing advantages, not shared by traditional linear analysis approaches, the necessity of a steep learning curve for effective utilization and correct interpretation of the results often slows down the adoption in applications [Hilborn, 2000; Strogatz, 2001].

In regards to the composition and behavior of the hippocampal EEG, the premise is that certain complex nonlinear behaviors such as the strange attractor can be examined by nonlinear dynamics analysis. The correlation dimension, for example, is one such quantifier measure of chaos that examines the geometric aspect of strange attractors and provides an estimate of the fractal microstructure dimension [Ding et al., 1993; Grassberger and Procaccia, 1993; Hilborn, 2000].

In our study, the correlation dimension was used to as a quantifier measure to compare the developmental differences of the hippocampal EEG measured from CA1 and the dentate gyrus during REM sleep between two age groups: 15 and 90 days. The correlation dimension measure was estimated using an in-house modified Grassberger and Procaccia (mGP) method. Our study has found that the estimated correlation dimensions of the theta activities in the hippocampal EEG at the dentate gyrus are significantly larger than those of CA1 in younger rats of 15 days of age. The difference in the correlation dimension measure between these two hippocampal subfields at the younger age, however, is insignificant in mature rats of 90 days of age.

2. Material and Methods

2.1. Correlation Dimension Estimation

In chaotic studies, the fractal dimension is classically defined as the exponent (D) that scales the object with squares, cubes or hyper-cubes of varying sizes (τ) [Hilborn, 2000; Strogatz, 2001],

$$B \propto \tau^{D} \tag{1}$$

where exponent

$$D \approx \lim_{\tau \to 0} \frac{\log(B)}{\log(\tau)} \tag{2}$$

In nonlinear dynamics and chaos, the correlation (fractal) dimension is a measure of active degrees of freedom and often derived from the trajectory of a strange attractor in many applications, where the phase space trajectory represents a graphical display of the time evolution of a dynamic system and from which certain properties of a dynamical system are captured. To facilitate the computation, Grassberger and Procaccia proposed an alternative to computing the fractal dimension by requiring only the computation of Euclidean distances between two state vectors. This algorithm leads to the computation of a *correlation integral* [Grassberger and Procaccia, 1993] shown below

$$C(\tau) = \frac{2}{N(N-1)} \sum_{i=1}^{N} \sum_{j=i+1}^{N} \Theta(\tau - \|\vec{v}(i) - \vec{v}(j)\|) \tag{3}$$

where Θ is the Heaviside function and ||.|| represents the Euclidean distance between two state vectors reconstructed in phase space using the time-delay embedding method [Takens, 1981] described below,

$$\vec{v}(i) = [x(i), x(i+L), \ldots x(i+(m-1)L] \tag{4}$$

where L is the delay time (lag) and *m* is the embedding dimension. The lag is to be chosen to make state vectors uncorrelated. $L=6$ was used in this study. The *correlation dimension* (D_2, also termed as *dimension complexity* by [Pritchard and Duke 1995]) is commonly estimated as the slope of the $\log C(\tau)$ vs. $\log(\tau)$ plot within a manually selected linear scaling region.

$$D_2 = \frac{\log C(\tau + d\tau) - \log C(\tau)}{\log(\tau + d\tau) - \log(\tau)} \tag{5}$$

2.2. Modified Grassberger-Procaccia Method

The computational load for $C(\tau)$ is rather heavy because a small step size ($\Delta\tau$) is usually used to increase the scaling variable τ; and, in order for $C(\tau)$ to converge, a large scaling range of τ sometime has to be covered. Due to time-delay embedding in reconstructing the state vector in (4), the Euclidean distance between two state vectors normally increases as the embedding dimension (*m*) does. As a remedy to make the correlation integral less sensitive to a varying embedding dimension, a modified G-P method was proposed [Ning et al., 2008] to normalize the Euclidean distance as the following,

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$$\left\| \vec{v}(i) - \vec{v}(j) \right\| = \sqrt{\frac{\sum_{k=0}^{m-1} [x(i+kL) - x(j+kL)]^2}{m}} \,. \tag{6}$$

The performance of mGP has been effectively proven in applications [Ning et al., 2008, 2009] and it has shown to be less sensitive to the varying embedding dimension. It's fair to mention that other *norms* different from the Euclidean norm also exist, such as the maximum norm and uniform norm, and they can also be adopted in (3) to measure the distances between state vectors. In this study, the normalized Euclidean norm in (6) was utilized. One major advantage of the mGP method [Ning et al., 2008] is that the convergence range remains essentially unchanged for varying embedding dimensions while the convergence ranges using the original GP method [Grassberger and Procaccia, 1993] increase as the embedding dimension does.

3. Results

The hippocampal EEG during sleep was recorded from rats of 15 and 90 days of age using electrodes implanted in the ipsilateral dentate granule cell layer and the CA1 pyramidal cell layer. Signals recorded from these hippocampal subfields were band-pass filtered (1 - 75 Hz) with a 60 Hz notch filter; REM sleep EEG segments of 8-second duration were manually selected. A minimum of thirty segments were selected and analyzed from each animal in this study.

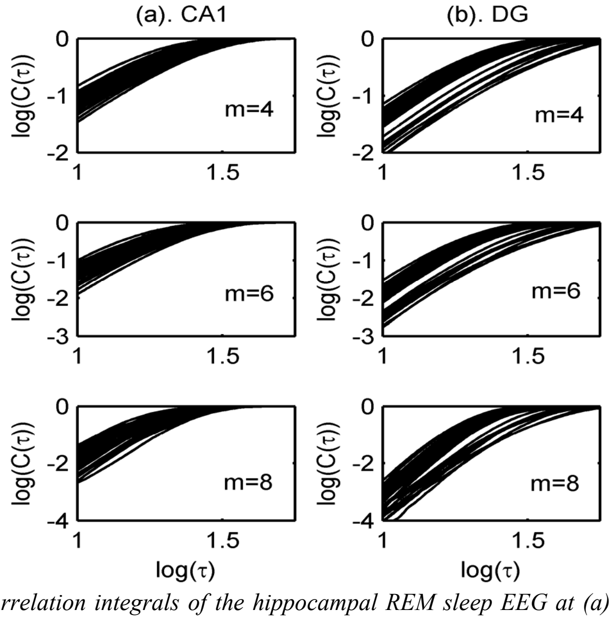

Figure 1. *Correlation integrals of the hippocampal REM sleep EEG at (a) CA1 and (b) the dentate gyrus for embedding dimensions m=4, 6, and 8 of a 15-day old rat.*

The mGP method was implemented via FORTRAN. Computation of C(τ) was performed to cover a range of τ within which C(τ) converges; the range was individually selected for each animal. Correlation integrals of a 15-day old rat are displayed in Fig.1 for three different embedding dimensions (*m*=4, 6, and 8). It's quickly noticed in Fig.1a that for the three different tested embedding dimensions, the plots of *log C(τ)* in CA1 converge to zero slower than those of DG displayed in Fig.1b. A linear scaling region (log(τ) ϵ [1.1,1.2]) to highlight the constant converging rate (slope) is displayed in Fig.2. In the chosen region, *log C(τ)* vs. *log(τ)* plots exhibit a relatively constant slope.

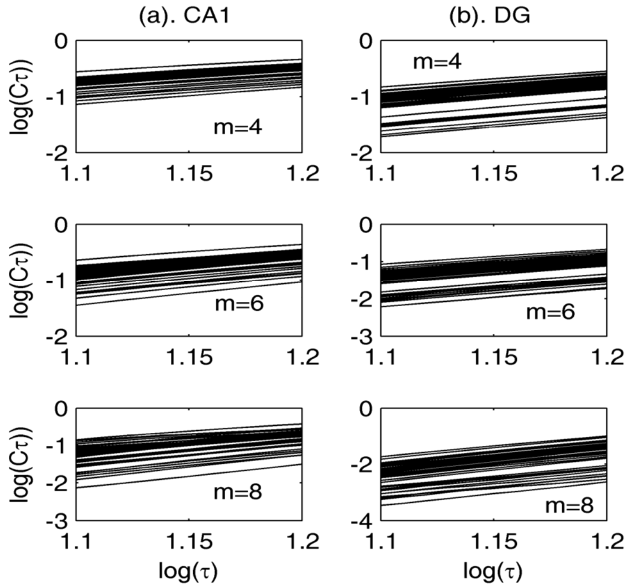

Figure 2. A linear scaling region of correlation integrals of hippocampal REM sleep EEG at (a) CA1 and (b) the dentate gyrus for embedding dimensions m=4, 6, and 8 of a 15-day old rat.

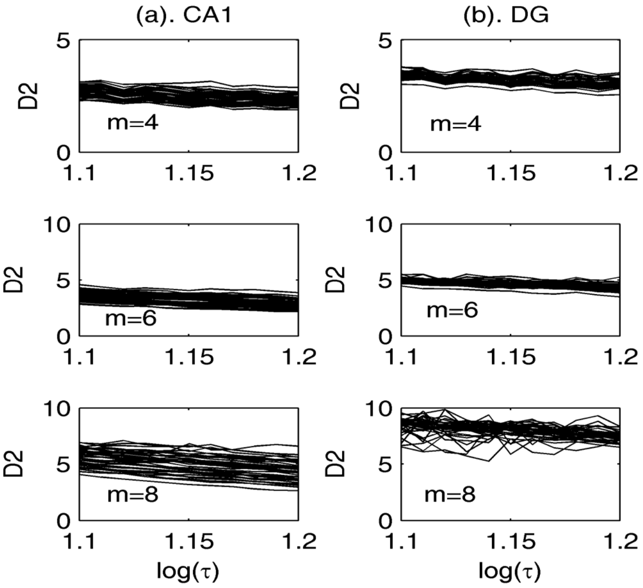

Figure 3. *Correlation dimension estimates of the hippocampal REM sleep EEG at (a) CA1 and (b) the dentate gyrus for embedding dimensions m=4, 6, and 8 of a 15-day old*

The correlation dimensions of the hippocampal EEG at CA1 and the dentate gyrus estimated in the linear scaling region are displayed in Fig.3. The correlation dimension estimates (D_2) of the EEG at DG are noticeably larger than CA1. While the choice of a linear scaling region is subject to an individual's bias and may affect the estimate, we found the aforementioned observation (i.e., D_2 of EEG at the dentate gyrus is larger than CA1 for rats of 15 days of age) holds when the linear scaling region was slightly varied. This observation provides another angle from the fractal dimension to interpret the existing physiological finding that the granule cells in the dentate gyrus develop rapidly after birth, or, alternatively, more complexity by the fractal dimension measure.

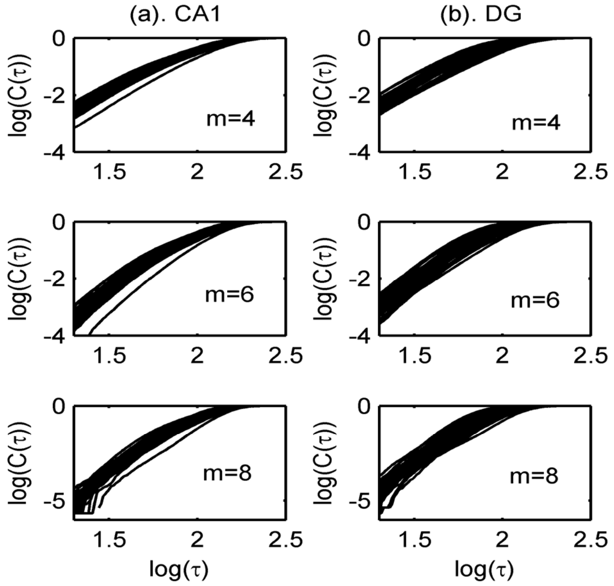

Figure 4. *Correlation integrals of the hippocampal REM sleep EEG at (a) CA1 and (b) the dentate gyrus for embedding dimensions m=4, 6, and 8 of a 90-day old rat.*

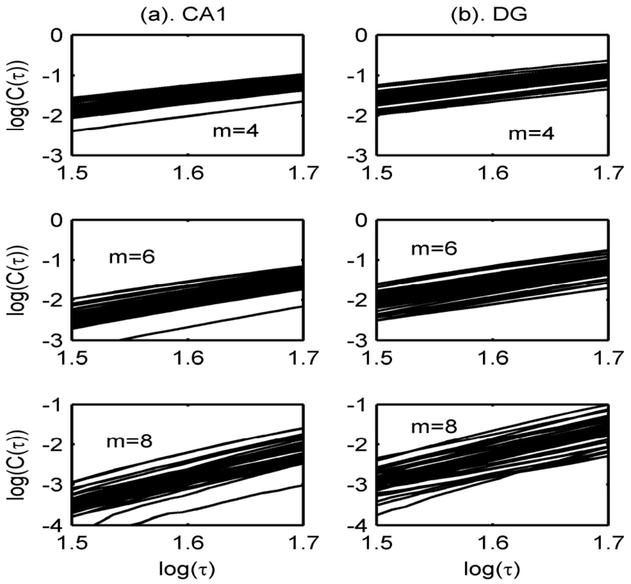

Figure 5. *A linear scaling region of correlation integrals of hippocampal REM sleep EEG at (a) CA1 and (b) the dentate gyrus for embedding dimensions m=4, 6, and 8 of a 90-day old rat.*

The correlation integrals of a 90-day old rat are shown in Fig.4. Unlike the situation in rats of 15 days of age(Fig.1), there is no noticeable difference between the correlation integral plots in CA1 (Fig.4a) and DG (Fig.4b). Correlation integrals of hippocampal EEG at CA1 and DG show similar patterns. A linear scaling region ($log(\tau) \in [1.5 \rightarrow 1.7]$) was selected from Fig.4 and correlation integrals in that region are displayed in Fig.5. There are no noticeable differences between $log\ C(\tau)$ plots of CA1 and the dentate gyrus. The correlation dimensions in the scaling region in Fig.5 were estimated and are shown in Fig.6, where D_2 values are clustered in similar ranges for embedding dimensions m = 4, 6, and 8 in both CA1 (Fig.6a) and DG (Fig.6b).

4. Discussion

Hippocampal EEGs collected from several animals in 15-day and 90-day age groups were analyzed; patterns and observations similar to Fig.1 through Fig.6 were repeated in each animal. To statistically characterize the developmental differences for each animal, means and standard deviations of the estimated correlation dimension are summarized in Table 1. The numbers in Table 1 provide strong evidence that the EEG theta activity recorded at the dentate gyrus is more chaotic than CA1 for young animals of 15 days of age; and the difference in correlation dimension measure diminishes as rats mature at 90 days of age. We reconfirmed the results by using different lag (L) values in reconstructing the state vectors in phase space and found no major changes in our findings. In addition, the preceding findings remain unchanged with slightly altered linear scaling regions.

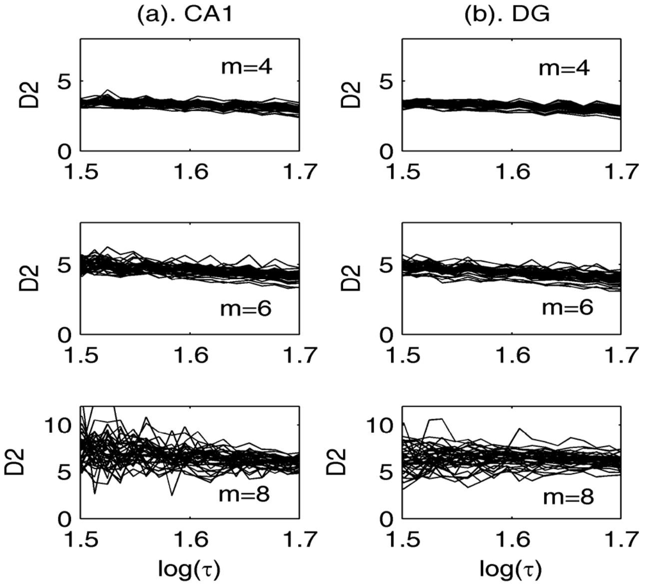

Figure 6. *Correlation dimension estimates of the hippocampal REM sleep EEG at (a) CA1 and (b) the dentate gyrus for embedding dimensions m=4, 6, and 8 of a 90-day old.*

Table 1. *Correlation dimension measures of the hippocampal EEG during REM sleep for rats of 15 and 90 days of age.*

Age	*Correlation Dimension*	*Mean ± STD*
15-day (animal-#1)	CA1	DG
m=4	2.503±0.238	3.222±0.166
m=6	3.216±0.423	4.599±0.234
m=8	3.863±0.591	5.886±0.275
15-day (animal-#2)		
m=4	2.930±0.479	3.315±0.236
m=6	3.667±0.750	4.682±0.411
m=8	4.451±0.963	5.869±0.563
90-day (animal-#1)	CA1	DG
m=4	3.348±0.159	3.266±0.159
m=6	4.645±0.261	4.479±0.269
m=8	5.683±0.341	5.429±0.371
90-day (animal-#2)		
m=4	3.126±0.147	3.103±0.141
m=6	4.217±0.250	4.205±0.248
m=8	5.063±0.325	5.131±0.325

5. Conclusions

The EEG activities were recorded from the hippocampal subfields—pyramidal cell layer at CA1 and the granule cell layer at the dentate gyrus—during REM sleep from freely moving rats of 15 and 90 days of age. The correlation dimension was used as the quantifier to compare the developmental changes between the EEG at CA1 and the dentate gyrus as animals mature. It was found in rats of 15 days of age that the estimated measures of correlation dimension at the dentate gyrus are significantly larger than those of CA1. On the other hand, for adult rats of 90 days of age, the correlation dimension measures exhibit no noticeable differences between CA1 and the dentate gyrus. This observation adds to our existing understanding (derived primarily through linear measures) of the ontogeny of the hippocampal EEG theta activity during REM sleep another perspective in regards to its nonlinear dynamics and chaotic behavior.

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