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Fractal Dimension of the EEG in Alzheimer's Disease

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INTRODUCTION

Alzheimer's disease (AD) is the most frequent cause of dementia in western countries, and is characterized by progressive impairments in cognition and memory, whose course lasts several years prior to death (Jeong, 2004). These clinical features are accompanied by histological changes in the brain, which include widespread cortical atrophy, intracellular deposition of neurofibrillary tangles, and extracellular deposition of senile plaques, particularly in the hippocampus and the cerebral cortex. Although a definite diagnosis is only possible by necropsy, a differential diagnosis with other types of dementia and with major depression should be attempted. Magnetic resonance imaging and computerized tomography can be normal in the early stages of AD, but a diffuse cortical atrophy is the main sign in brain scans. Mental status tests are also useful.

The analysis of the electromagnetic brain activity can provide important information to help in the diagnosis of several mental diseases. The electroencephalogram (EEG) has been used as a tool for diagnosing dementias for several decades. The hallmark of EEG abnormalities in AD patients is a shift of the power spectrum to lower frequencies, and a decrease of coherence among cortical areas (Jeong, 2004).

Recent progress in the theory of nonlinear dynamics has provided new methods for the study of the EEG (Jeong, 2004). Nonlinearity is found in the brain even at the cellular level. Given the highly nonlinear nature of the neuronal interactions, the EEG appears to be an appropriate area for nonlinear time series analysis.

BACKGROUND

There are many studies in which the EEG has been studied with nonlinear time series analysis techniques. These investigations have revealed possible medical applications, since analysis based on nonlinear dynamics yields information unavailable from traditional EEG spectral-band analysis (Pritchard, Duke, Coburn, Moore, Tucker, Jann, & Hostetler, 1994). Moreover, they have given rise to the possibility that the underlying mechanisms of the brain function may be explained by nonlinear dynamics (Röschke, Fell, & Beckmann, 1995; Stam, Jelles, Achtereekte, Rombouts, Slaets, & Keunen, 1995). Particularly, several studies have examined the nonlinear dynamics of the EEG in AD. It has been found that AD patients have lower correlation dimension (D_2) values—a measure of dimensional complexity of the underlying system—than control subjects (Jeong, Chae, Kim, & Han, 2001; Jeong, Kim, & Han, 1998; Pritchard et al., 1994; Stam et al., 1995). The first Lyapunov exponent ($L1$) has also been used to characterize nonlinear behavior. AD patients have significantly lower $L1$ values than controls in almost all EEG channels (Jeong et al., 1998; Jeong et al., 2001a). However, the amount of data required for meaningful results in the computation of D_2 and $L1$ is beyond the experimental possibilities for physiological data (Eckmann & Ruelle, 1992). Thus, different nonlinear techniques are needed to study the EEG background activity.

Mutual information analysis (Jeong, Gore, & Peterson, 2001) has been used to assess information transmission between different cortical areas in AD. Furthermore, some studies have confirmed the decrease of EEG complexity in AD with suitable nonlinear techniques like Lempel-Ziv's complexity (Abásolo, Hornero, Gómez, García, & López, 2006) or multiscale entropy (Escudero, Abásolo, Hornero, Espino, & López, 2006).

As it can be noted, very different nonlinear analysis techniques have been proposed to analyze the EEG background activity in AD patients, although some of them are not suitable to study biomedical signals. In this study, we have evaluated the usefulness of the fractal dimension (*FD*) to characterize the AD patients' EEG background complexity.

FRACTAL DIMENSION OF THE EEG BACKGROUND ACTIVITY

EEG Recording

Ten patients (four men and six women; age = 74.80 ± 3.94 years, mean ± standard deviation (SD)) fulfilling the criteria of probable AD were recruited from the Alzheimer's Patients' Relatives Association of Valladolid (AFAVA) and referred to the University Hospital of Valladolid (Spain), where the EEG was recorded. All of them had undergone a thorough clinical evaluation that included clinical history, physical and neurological examinations, brain scans, and a Mini-Mental State Examination (MMSE), generally accepted as a quick and simple way to evaluate cognitive function (Folstein, Folstein, & McHugh, 1975). The mean MMSE score for the patients was 13.1 ± 5.9 (Mean ± SD).

The control group consisted of 10 age-matched, elderly control subjects without past or present neurological disorders (six men and four women; age = 73.10 ± 6.37 years, mean ± SD). The MMSE score value for all control subjects was 30. All control subjects and all caregivers of the patients gave their informed consent for participation in the current study, which was approved by the local ethics committee.

More than five minutes of data from the 19 scalp loci of the international 10-20 system (electrodes Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, T6, Fz, Cz, and Pz) were recorded from each subject using a Profile Study Room 2.3.411 EEG equipment (Oxford Instruments). Sample frequency was 256 Hz, with a 12-bit A-to-D precision. Recordings were made with subjects in a relaxed state, and under the eyes-closed condition, to obtain as many artifact-free EEG data as possible. All EEGs were visually inspected by a specialist physician, and only EEG data free from electrooculographic and movement artifacts, and with minimal electromyographic (EMG) activity were selected. EEGs were organized in five-second artifact-free epochs (1280 points). Furthermore, prior to the *FD* analysis, all recordings were digitally filtered with a band-pass filter with cut-off frequencies at 0.5 Hz and at 40 Hz to remove residual EMG activity.

Fractal Dimension

Fractal geometry is a new language used to describe, model, and analyze complex forms or curves found in nature. Whereas Euclidean shapes have one, or at most a few, characteristic sizes or length scales, fractals, like a coastline, possess no characteristic sizes, and are said to be self-similar and independent of scaling (Accardo, Affinito, Carrozzi, & Bouquet, 1997). A fractal curve in an n-dimensional space has topological dimension n, and a noninteger or fractional dimension called fractal dimension (*FD*). It also possesses the characteristic that each portion of it can be considered a reduced-scale image of the whole for all time scales. If the scaling factor is the same for all time scales, then the curve is said to be self-similar. Many algorithms developed to estimate the *FD* are based on the assumption of self-similarity and independence of scaling (Esteller, Vachtsevanos, Echauz, & Litt, 1999).

FD can be considered a relative measure of signal complexity (Accardo et al., 1997; Katz, 1988). It provides an alternative technique for assessing signal complexity in the time domain, as opposed to the embedding method of assessing this complexity by reconstructing the attractor in the multidimensional phase space, something that is a notable advantage over traditional chaotic techniques, such as D_2 (Accardo et al., 1997). Furthermore, *FD* can characterize different pathophysiological conditions, and it has been particularly useful in the analysis of EEG to