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Spatiotemporal nonlinearity in resting-state fMRI of the human brain

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In this work, the spatiotemporal nonlinearity in resting-state fMRI data of the human brain was detected by nonlinear dynamics methods. Nine human subjects during resting state were imaged using single-shot gradient echo planar imaging on a 1.5T scanner. Eigenvalue spectra for the covariance matrix, correlation dimensions and Spatiotemporal Lyapunov Exponents were calculated to detect the spatiotemporal nonlinearity in resting-state fMRI data. By simulating, adjusting, and comparing the eigenvalue spectra of pure correlated noise with the corresponding real fMRI data, the intrinsic dimensionality was estimated. The intrinsic dimensionality was used to extract the first few principal components from the real fMRI data using Principal Component Analysis, which will preserve the correct phase dynamics, while reducing both computational load and noise level of the data. Then the phase-space was reconstructed using the time-delay embedding method for their principal components and the correlation dimension was estimated by the Grassberger-Procaccia algorithm of multiple variable series. The Spatiotemporal Lyapunov Exponents were calculated by using the method based on coupled map lattices. Through nonlinearity testing, there are significant differences of correlation dimensions and Spatiotemporal Lyapunov Exponents between fMRI data and their surrogate data. The fractal dimension and the positive Spatiotemporal Lyapunov Exponents characterize the spatiotemporal nonlinear dynamics property of resting-state fMRI data. Therefore, the results suggest that fluctuations presented in resting state may be an inherent model of basal neural activation of human brain, cannot be fully attributed to noise.

Keywords: Spatiotemporal nonlinearity; Correlation dimension; Spatiotemporal Lyapunov Exponents; Intrinsic dimensionality; Principal Component Analysis; fMRI; Resting-state; Human brain

Introduction

Functional magnetic resonance imaging (fMRI) has emerged as a useful and noninvasive technique for the study of structure-function relationship in the human brain. Using magnetic resonance techniques, researchers have found that it is possible to indirectly detect changes in blood-oxygenation levels that are a result of neuronal activation. In the past decade interest in this novel research field increased rapidly. Most of the work concentrated on the detection or the estimation of brain regions involved in specific cognitive or sensor-motor tasks.

The complex behavior of the hemodynamic response is a global phenomenon and the reconstruction of the dynamics recorded in fMRI data should make use of the vast amount of spatial information acquired (Laird et al., 2002). Spatiotemporal electroencephalography (EEG) and magnetoencephalography (MEG) signal analysis can achieve higher performance by combining spatial and temporal approaches (Lee and Kim, 2006; Uhl et al., 1998; Pezard et al., 1996). Compared with EEGs of low spatial resolution, fMRI data offer millimeter spatial resolution (1 to 4 mm) with temporal resolutions of the order of seconds. It can offer more spatial information than EEG/MEG. Hence, spatiotemporal analysis by fMRI will produce an important analytic tool for brain research (McIntosh et al., 2004).

Conscious rest has been widely used as a baseline condition in neuroimaging experiments such as positron emission tomography (PET) and functional magnetic resonance imaging (Gusnard and Raichle, 2001). In most cases, rest state is defined as a state that differs from the active state both in terms of conditions (open/closed eyes, absence/presence of a stimulus input) and instructions given to the subject (Wicker et al., 2003). A rest state can therefore be used in a wide variety of experiments. However, it is an ill-defined mental state because it may vary both from one subject to another and within the same subject (Luca et al., 2006; Wicker et al., 2003).

Extracting information from resting-state is a challenging work, because the signals of interest are contaminated by physiological noise, such as breathing, cardiac activity (Thirion et al., 2006) and scan noise. Many methods are introduced to analyze resting-state fMRI data, such as Fourier Transformation (Cordes et al., 2001), Correlation Analysis (Hampson et al., 2002; Cordes et al., 2001; Lowe et al., 1998), Principal Component Analysis (Worsley et al., 2005; Zuendorf et al., 2003), and Independent Component Analysis (Luca et al., 2006; Bartels and Zeki, 2005). However,

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the majority of methods developed for resting-state fMRI data analysis so far are linear in nature.

Recently, the analysis of human EEGs with methods based on nonlinear dynamics and chaos theory has become increasingly popular (Lehnertz and Elger, 1998; Pezard et al., 1996). One of the most important contributions of nonlinear dynamics to the general view of the physical world is the message that irregular and seemingly unpredictable behaviors do not necessarily have to be attributed to some random external inputs to the systems, but on the contrary can be the result of completely deterministic dynamical systems (nonlinearity is a necessary). This new paradigm offers a possible new way to the analysis of many irregular time series, which have been regarded only as stochastic signals before the breakthrough of nonlinear dynamics (Galka, 2000). The application of nonlinear dynamics analysis tools to characterize time series may provide a more complete description of EEG recordings (Stam, 2005; Lee et al., 2001). It has been regarded as an important advance in understanding the underlying mechanism of brain electrical activities. It has been realized that if chaos could be demonstrated in a natural system, such as the human brain, it might provide a much simpler explanation for the occurrence of complex behavior than usual stochastic models (Lee et al., 2001). The presence of nonlinear or deterministic chaotic behavior in various physiological and pathological states has been postulated, but also disputed (Freeman, 2000; Stam et al., 1995). Therefore, detection of nonlinearity is important and should be the first step before any nonlinear analysis.

Even though there is an effort to study nonlinear dynamics of brain activities using EEG, very little research has been done in applying methods of nonlinear dynamics to fMRI data, particularly during resting state of the human brain. Recently, the nonlinear dynamics analysis of fMRI data of the human brain has begun to attract many researchers. An extension of the delta-epsilon approach is applied to fMRI data to evaluate whether a time course of a candidate voxel provides additional information concerning the time evolution of reference voxel time series (LaConte et al., 2004). The nonlinearity arising from the finite dimensional dynamics are then characterized using patterns of singularities in the complex plane. A finite embedding dimension is a measure of the determinism of the system, which can be quantified using information theoretic measures like Lempel-Ziv complexity (Deshpande et al., 2006). Using spatial embedding of fMRI data, local spatiotemporal chaos in baseline (Deshpande et al., 2005) has been reported. However, most works on nonlinear analysis to fMRI data are taken voxel by voxel based on single time series (Gautanma et al., 2003), as is traditionally done in the nonlinear signal processing literature. On the other hand, though recent studies (Vazquez and Noll, 1998; Birn et al., 2001; Bandettini et al., 2002; Pfeuffer et al., 2003; Huettel, 2004) indicate the nonlinear nature of fMRI response to some stimulation and many nonlinear models between stimulations and their fMRI responses are established (Wager et al., 2005; Harrison et al., 2003; Friston et al., 2000; Buxton et al., 1998), these results are obtained by means of stimulations and their fMRI responses. However, in resting-state of the human brain, there are no significant stimulations. Hence, it is difficult to detect the nonlinearity by way of stimulations and their fMRI responses.

In this work, the nonlinearity in resting-state fMRI signals of the human brain was detected using two methods which are usually used to characterize the essence of a nonlinear dynamical system. One is the correlation dimension analysis which analyzes quantitatively the nonlinear fractal property of fMRI data of the human brain. Another is the Spatiotemporal Lyapunov Exponent (STLE) analysis which characterizes the nonlinear chaotic property of fMRI data of the human brain.

Because various dynamical quantities of the reconstructed set or phase-space are the same as those of the underlying attractor (Kantz and Schreiber, 1997), provided that embedding dimension is suitably large, an appropriate phase-space reconstruction has to be carried out before estimating the correlation dimension of fMRI data using Grassberger-Procaccia algorithm. The so-called "appropriate" is that the reconstructed set not only comprises essential information and noise-free, but also has appropriate calculation quantity and as less redundancy as possible. So knowing the essential number of signal components is a key step for popular fMRI data post-processing.

In order to estimate accurately the number of essential signals for the resting-state fMRI data of the human brain, i.e. the intrinsic dimension, a method based on an autoregressive noise model of order 1, AR(1) noise model, was used to estimate the intrinsic dimensionality of fMRI data and cubic spline interpolation was introduced to the estimate of AR(1) coefficient ϕ. According to the estimated intrinsic dimensionality, the principal components of fMRI data were extracted by Principal Component Analysis (PCA) method. The phase-space was reconstructed using the time-delay embedding method for their principal components. In the reconstructed phase-space, the correlation dimension of spatiotemporal series was estimated using Grassberger-Procaccia algorithm. The important result of fractal correlation dimension characterizes quantitatively the nonlinear fractal property of resting-state fMRI data of human brain.

On the other hand, the global coupled STLE, which is based on coupled map lattices (CML), was introduced to analyze spatiotemporal series of fMRI data in resting-state of human brain. The result of positive STLE, which characterizes the chaotic nonlinear dynamical property, was also obtained.

In the end, two kinds of surrogate data generated from raw fMRI data were introduced to test the nonlinearity in resting-state fMRI data of human brain.

Material and methods

Correlation dimension analysis

Correlation dimension

The correlation dimension is a method aiming at practical applications where the geometrical object has to be reconstructed from a finite sample of data points which mostly contain some errors as well. The Grassberger-Procaccia algorithm (Kantz and Schreiber, 1997; Hegger and Kantz, 1999), which is the most popular method to estimate the correlation dimension, is based on an appropriate phase-space reconstruction. One of the most popular methods for phase-space reconstruction is time-delay embedding (Bianciardi et al., 2007; Perc, 2005; Cellucci et al., 2003; Hegger and Kantz, 1999). Given a scalar time series $x(t)$, a sequence of vectors $y(t)=(x(t),x(t+\tau),\cdots,x(t+[m-1]\tau))$ is formed, where m is embedding dimension and τ is the delay time. Thus, a phase space of m dimensions is reconstructed by this sequence of vectors. Under quite general circumstances the attractor formed by delay embedding is equivalent to the attractor in unknown space in which the underlying dynamical system is living if the embedding dimension m of the delay coordinate space is sufficiently large.

Meanwhile it is assumed that there are only a finite number of points which are generated by a dynamic system. After phase space