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The multiscale character of evoked cortical activity

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Both the architecture and the dynamics of the brain have characteristic features at different spatial scales. However, the existence, nature and function of dynamical interdependencies between such scales have not been investigated. We studied the multiscale properties of functional magnetic resonance imaging (fMRI) data acquired while human subjects viewed a visual image. Traditional "region of interest" analysis of this data set revealed evoked activity in primary and extrastriate visual cortex. Wavelet transform in the spatial domain provides a multiscale representation of this evoked brain activity. Studying the correlation structure of this representation revealed strong and novel interdependencies in these data within and between different spatial scales. We found that such correlations are stronger than those evident in the original data and comparable in magnitude to those obtained after Gaussian smoothing. However, analysis of the data in the wavelet domain revealed additional structure such as positive correlations, strong anti-correlations and phase-lagged interdependencies. Statistical significance of these effects was inferred through nonparametric bootstrap techniques. We conclude that the spatial analysis of functional neuroimaging data in the wavelet domain provides novel information which may reflect complex spatiotemporal neuronal activity and information encoding. It also affords a quantitative means of testing hierarchical and multiscale models of cortical activity.

Keywords: Functional connectivity; Neural dynamics; Wavelet analysis; Neurovascular coupling; Complexity

Introduction

Neuroimaging technologies permit the neural correlates of sensory processing, cognitive activity and motor behavior to be topographically mapped in an increasingly precise manner. However, the spatiotemporal dynamics of such neural responses have remained elusive. That is, the "where" of neural processing is being increasingly well documented, but, in contrast, the dynamical structure of this activity is less understood. Improving the characterization of task-related neuronal dynamics offers great potential in better elucidating its representational and computational attributes. The aim of this paper is to present an exploratory study of the dynamical structure of visually evoked cortical activity in fMRI data through the use of the wavelet transform. The wavelet transform permits the spatiotemporal properties of a data set to be quantitatively mapped. We hypothesize that such a multiscale representation will reveal novel features of the data that cannot be captured by existing methods and which reflect computational aspects of neural activity.

A common approach to the analysis of fMRI data is to apply a Gaussian filter in the spatial domain as a preprocessing step. This technique has proven remarkably successful in improving the "signal-to-noise" ratio. However, implicit in such a step is an assumption concerning the spatial properties of both the signal and the noise components of the data. Moreover, because of its broad spectral character, a Gaussian filter captures activity across a broad range of spatial scales. There are several reasons to consider that neural responses may have scale-specific properties: (1) one of the over-arching organizational principles of the brain's architecture appears to be the segregation of neuronal tissue into densely interconnected subsystems across a hierarchy of spatial scales—from microcolumns (~40 μm) (Nunez, 1997) through cortical columns (0.3–3 mm) (Szentagothai, 1983; Mountcastle, 1997; Shephard, 2004) to cortical subareas, areas and hemispheres (Hilgetag et al., 2000; Stephan et al., 2001; Passingham et al., 2002). (2) Information–theoretical considerations argue that the complexity and robustness of neuronal processes may be optimized when there exist strong statistical interdependencies between subsets of a neuronal system across many spatial (Tononi et al., 1994, 1999) and temporal (Breakspear, 2002) scales. (3) Neocortical dynamics have been

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modeled as an ensemble of coupled nonlinear subsystems (Frank et al., 2000) which exhibit a rich repertoire of multiscale effects in both the spatial (Kaneko, 1994; Nakao et al., 2001) and temporal (Fujimoto and Kaneko, 2003) domains. Where such effects are temporally asymmetric, they have the character of a cascade, permitting microscopic events to influence macroscopic outcomes. Such mechanisms could facilitate information flow between feature-specific neurons in primary sensory cortex and distributed large-scale activity at higher levels of the cortical hierarchy (Mesulam, 1998; Breakspear and Stam, 2005).

The putative existence of scale-specific effects is an empirical question that requires special data analysis techniques. Employing Gaussian filters with different center frequencies is not a suitable approach as it is not possible to uniquely and/or fully represent the data in such a way. Wavelet functions, on the other hand, form a complete orthonormal basis set which is optimized for precisely such a purpose. In this paper, a wavelet-based correlation analysis is employed in an exploratory analysis of fMRI data acquired while human subjects viewed a flickering visual stimulus presented in a periodic block design. The choice of this paradigm is informed by the objective to characterize evoked neural activity as it enters the visual stream through primary striate cortex—that is, we seek to understand the multiscale representation of a very basic visual stimulus. The visual cortical regions identified by applying traditional data analysis methods to such an experimental paradigm have been extensively documented, including the data analyzed in the present study (Williams et al., 2000). The existence of more complex structure within such data is therefore an intriguing empirical question. The aim of this paper is to test the hypothesis that a multiscale representation of the data will reveal the existence and scale-characteristics of the evoked activity without the a priori constraints imposed by pre-smoothing.

Methodology

Wavelet decomposition

A wavelet family $\mathbf{W}_{j,k}(\mathbf{x})$ is a set of orthogonal basis functions which permit a complete linear decomposition of a data set $\mathbf{S}(\mathbf{x})$,

$$\mathbf{S}(\mathbf{x}) = \sum_{j,k} \mathbf{W}_{j,k}(\mathbf{x}) d_{j,k} \tag{1}$$

where j indexes scale and k indexes position. The family of wavelet functions $\mathbf{W}_{j,k}$ $(\mathbf{x})$ are generated through dilation (by j) and translation (by k) of a single "mother" wavelet function $\mathbf{W}(\mathbf{x})$ (Daubechies, 1992; Mallat, 1999). The "detail coefficients" $d_{j,k}$ are calculated as the inner product of the corresponding wavelet function and the data,

$$d_{j,k} = \langle \mathbf{W}_{j,k}(\mathbf{x}), \mathbf{S}(\mathbf{x}) \rangle_\Omega = \int_\Omega \mathbf{W}_{j,k}(\mathbf{x}) \mathbf{S}(\mathbf{x}) \mathrm{d}\mathbf{x} \tag{2}$$

where $\boldsymbol{\Omega}$ denotes the domain of $\mathbf{S}$. The wavelet decomposition yields a representation of the variance of the data across a hierarchy of scales $j = 1, 2, 3\ldots$. These have the dyadic structure $N_j = 2^n N_{j+n}$ where N_j denotes the number of elements at scale j. For two-dimensional data, there are three sets of detail coefficients at each scale, representing the variance in the horizontal d^h, vertical d^v, and diagonal d^d directions. These have two translation factors k and l accounting for the two spatial dimensions.

Principle methodology: wavelet-based correlation analysis

Given the time series of a spatially extended signal $\mathbf{S}(\mathbf{x}, t_i)$, then a spatial wavelet transform of the data at each time point yields the wavelet coefficient time series $d_{j,k}(t_i)$. A wavelet-based correlation analysis (as proposed by Arneodo et al., 1998; Nakao et al., 2001) simply examines the correlation and cross-correlation functions defined on these spatial wavelet coefficients. These are performed after the spatial location of the wavelet coefficients are determined, taking into account the dyadic downsampling at successive scales.

Two-region correlations

We first define the inter-scale correlation function for effects occurring between two points. At each scale j and for each set of coefficients, define the coarse-grained field $b_j(\mathbf{x}, t)$ as

$$b_j^a(\mathbf{x},t) = d_{j,k,l}^a(t) \tag{3}$$

where

$$\left(\left(\frac{k}{2^j}, \frac{l}{2^j} \right) \leq \mathbf{x} \leq \left(\frac{k+1}{2^j}, \frac{l+1}{2^j} \right) \right), \tag{4}$$

for $k, l = 0, 1, \ldots, 2^j - 1$ and a indices either horizontal $a = h$, vertical v or diagonal d coefficients. This captures the variance in signal intensity at a certain position $\mathbf{x}$, time t and scale j, accounting for the downsampling mentioned above. The deviations of these values from their mean values are given by

$$B_j^a(\mathbf{x},t) = b_j^a(\mathbf{x},t) - \frac{\langle b_j^a(\mathbf{x},t), I \rangle_T}{T}, \tag{5}$$

where I is a constant valued function $I(\mathbf{x}, t) \equiv 1$ and T is the total recording time. Define the wavelet cross-correlation matrix between positions $\mathbf{x}_1$ and $\mathbf{x}_2$ as

$$C_{j_1, j_2}^a(\mathbf{x}_1, \mathbf{x}_2, \Delta t) = \frac{\left\langle B_{j_1}^a(\mathbf{x}_1, t), B_{j_2}^a(\mathbf{x}_2, t+\Delta t) \right\rangle_T}{\sqrt{\left\langle B_{j_1}^a(\mathbf{x}_1, t), B_{j_1}^a(\mathbf{x}_1, t) \right\rangle_T \left\langle B_{j_2}^a(\mathbf{x}_2, t+\Delta t), B_{j_2}^a(\mathbf{x}_2, t+\Delta t) \right\rangle_T}} \tag{6}$$

This expresses the temporal correlation in the fluctuations of image intensity across spatial scales j_1 and j_2 with time lag Δt. In this exploratory analysis, we are interested in two aspects of this multivariate function. Firstly, we calculate the time-zero correlations $C_{j1,j2}^a(\mathbf{x}_1,\mathbf{x}_2,0)$. These values give the "instantaneous" inter-scale correlation between regions centered at $\mathbf{x}_1$ and $\mathbf{x}_2$. Secondly, we wish to study the entire functions and how these reflect the experimental paradigm. Each of these requires slightly different statistical approaches, which are described in the Statistical analysis section, below.

Single region multiscale correlations

By substituting $\mathbf{x}_1 = \mathbf{x}_2 = \mathbf{x}$ into Eq. (6), one obtains an expression for cross-scale correlations with a region centered at single location $C_{j1,j2}^a(\mathbf{x},\Delta t)$. Note that, when $\mathbf{x}_1 = \mathbf{x}_2$ and $\Delta t = 0$, the two terms on the numerator of Eq. (6) commute, and hence this matrix is symmetric, $C_{j1,j2}^a(\mathbf{x},0) = C_{j2,j1}^a(\mathbf{x},0)$. When $\Delta t > 0$, the matrix is asymmetric to a degree that can be exploited to