Monofractal and Multifractal Dynamics of Low Frequency Endogenous Brain Oscillations in Functional MRI

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Abstract: Fractal processes, like trees or coastlines, are defined by self-similarity or power law scaling controlled by a single exponent, simply related to the fractal dimension or Hurst exponent (H) of the process. Multifractal processes, like turbulence, have more complex behaviours defined by a spectrum of possible local scaling behaviours or singularity exponents (h). Here, we report two experiments that explore the relationships between instrumental and cognitive variables and the monofractal and multifractal parameters of functional magnetic resonance imaging (fMRI) data acquired in a no-task or resting state. First, we show that the Hurst exponent is greater in grey matter than in white matter regions, and it is maximal in grey matter when data were acquired with an echo time known to optimise BOLD contrast. Second, we show that latency of response in a fame decision/facial encoding task was negatively correlated with the Hurst exponent of resting state data acquired 30 min after task performance. This association was localised to a right inferior frontal cortical region activated by the fame decision task and indicated that people with shorter response latency had more persistent dynamics (higher values of H). Multifractal analysis revealed that faster responding participants had wider singularity spectra of resting fMRI time series in inferior frontal cortex. Endogenous brain oscillations measured by fMRI have monofractal and multifractal properties that can be related to instrumental and cognitive factors in a way, which indicates that these low frequency dynamics are relevant to neurocognitive function. *Hum Brain Mapp* 29:791–801, 2008. © 2008 Wiley-Liss, Inc.

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INTRODUCTION

Many biological systems, including the brain, have fractal properties in space and time [Achard et al., 2008; Anderson et al., 2006; Goldberger et al., 2002; Havlin et al., 1999; Maxim et al., 2005; Wright et al., 2001]. The characteristic attribute of a fractal process is self-similarity, i.e., the properties of a fractal process will be at least approximately the same over a range of scales of magnification [Bovill, 2000; Fielding, 1992].

Fractal signals are typically long-memory processes with a slowly decaying autocorrelation function [Bullmore et al., 2004; Fielding, 1992]. In the frequency domain, this corresponds to a $1/f$ -like spectral density function, with the lower frequencies having greater power and the slope of a straight line fitted to the log periodogram being defined as the spectral exponent, i.e., $S(f) \sim f^\gamma$ or $\log S(f) \sim \gamma \log f$. The spectral exponent γ is simply related to the fractal dimension D and the Hurst exponent, H , of the process [see Bullmore et al. [2004] for general review].

It has already been shown that functional MRI time series demonstrating blood oxygenation level-dependent (BOLD) contrast are fractal with $1/f$ -like power spectra [Maxim et al., 2005; Woolrich et al., 2001; Zarahn et al., 1997] and can be well modelled as fractional Gaussian noise with $0.5 < H < 1$ [Fadili and Bullmore, 2002; Maxim et al., 2005]. The Hurst exponent has previously been estimated from fMRI experiments where participants were scanned in a single consistent state, for example, during continuous performance of an emotional task [Anderson et al., 2006] or while lying quietly at rest in the scanner [Maxim et al., 2005; Wink et al., 2006]. The Hurst exponent of steady-state fMRI time-series is known to be sensitive to acute pharmacological challenge [Wink et al., 2006], early Alzheimer's disease [Maxim et al., 2005] and attention deficit-hyperactivity disorder [Anderson et al., 2006]. These studies suggest that long-memory dynamics in fMRI are relevant to cognitive function and could represent the hemodynamically convolved signature of very slow (infra-slow; < 0.1 Hz) oscillations of neuronal ensembles [Leopold et al., 2003; Vanhatalo et al., 2004]. Nevertheless, prior studies have not related fractal measures of BOLD time-series to behavioural or other independently recorded measures, which would provide additional evidence of the cognitive origins for observed changes. Furthermore, there are many other potential causes of $1/f$ -like noise, including cardiorespiratory and instrumental factors [Birn et al., 2006; Cordes et al., 2001]; so, the neurocognitive significance of long-memory in fMRI is not yet fully resolved.

It is also important to recognise that using the Hurst exponent (a single scalar) to summarise the properties of a time-series entails the implicit assumption that the process is monofractal, i.e., its scaling properties are stationary over time. However, the signature of turbulent physical [Argoul et al., 1989] and biophysical [Goldberger et al., 2002] systems is their non-stationarity and non-linearity and in these circumstances the Hurst exponent may be

insufficient as a summary statistic for the overall behaviour of the process. A more complete description is then provided by a multifractal formalism in which the local scaling behaviour in the neighbourhood of a singularity is characterised by a Hölder exponent, and the singularity spectrum or distribution of Hölder exponents over all singularity components in the signal summarises its multifractal behaviour [Muzy et al., 1993; Turiel et al., 2006].

Multifractal analysis has previously been applied to fMRI time-series recorded during periodic experimental stimulation and significant differences have been demonstrated in the singularity spectra of activated compared to non-activated brain regions [Shimizu et al., 2004]. However, the complexity of the neuronal processes refracted via the hemodynamic response, and detected by fMRI, makes a multifractal analysis potentially of interest in the characterisation of endogenous dynamics recorded while participants are in a no-task or resting state. A multifractal analysis of resting fMRI data has not yet been reported.

Here, we describe a number of fMRI experiments that were designed to further elucidate the neurophysiological origins of long-memory in endogenous brain dynamics. Firstly, we reasoned that if long-memory properties of fMRI time-series reflect low frequency neuronal activity of the brain, we would expect greater persistence—greater autocorrelation over longer time-lag or, equivalently, a higher value of H —in grey matter regions (where neuronal cell bodies are concentrated) than in white matter or CSF regions, and in data acquired with echo times (TE) that are optimal for the BOLD contrast. We tested these predictions in fMRI data acquired while TE was systematically varied in the range 22.5–100 ms. Secondly, we addressed the important question of how low frequency endogenous dynamics might relate to cognitive performance by investigating associations between response latency on a fame decision task and fractal properties of resting state data recorded about 30 minutes after task performance.

MATERIALS AND METHODS

Monofractals and the Hurst Exponent

A fractal process has the characteristic property of self-similarity, self-affinity or scale-invariance, i.e., it appears at least approximately the same over several scales of measurement. To take a single example of a natural fractal, the rough Atlantic coastline of Norway has sea inlets (fjords) on multiple different scales and the relationship between the measured length of the coast L and the scale r on which it is measured follows a power law:

$$L \propto r^{1-D} \quad (1)$$

where the fractal (Hausdorff) dimension, D , of the coastline ≈ 1.52 [Feder, 1988]. As in this case, when a single scaling exponent adequately describes the behaviour of a process, it is said to be a monofractal.

Figure 1.

Monofractal analysis of endogenous fMRI oscillations. (a) An illustrative fMRI time series, with time measured in images, and $TR = 1.1$ s; (b) its autocorrelation function; (c) top panel: its power spectrum, $S(f)$, on a logarithmic axis across wavelet scales; (c) bottom panel: the coefficients of its wavelet transform at each scale; the log variances at each scale (open circles) are plotted above the corresponding wavelet coefficients along with the regression line (solid line), the slope of which is an estimator of the Hurst exponent, H . Dashed lines denote the origins of the vertical-axes.

The empirical evidence for long-memory of fMRI signals (Fig. 1a,b) suggests that fractional Gaussian noise is a good candidate to model the observed auto-covariance [Maxim et al., 2005]. In this model, two parameters are necessary to fully specify the behaviour of the auto-covariance: the signal variance, σ^2 , and the Hurst exponent, H . If $0 \leq H < 0.5$, the auto-covariance is negative and the signal is anti-correlated; whereas, if $0.5 < H \leq 1$, then the auto-covariance is positive and the signal has long-memory or positive autocorrelations over long time lags (Fig. 1a,b).

For a long-memory process, a logarithmic plot of spectral power versus frequency (the log periodogram, Fig. 1c) shows a linear decrease in power with increasing frequency. The gradient of the log periodogram is the

spectral exponent, γ , which can be used to estimate H [Lowen and Teich, 1993; Ninness, 1998]. The fractal dimension D is also simply related to the Hurst exponent by the relation $D = 2 - H$ [Gneiting and Schlather, 2004; Schroeder, 1991].

There are alternative estimators of H in the wavelet domain with low bias and high efficiency [Fadili and Bullmore, 2002; Mallat 1989; Maxim et al., 2005]. From the bandpass property of the wavelet filters [Wornell, 1993], it follows that for a discrete signal with a $1/f$ -like power spectrum, the wavelet coefficients at each scale are decorrelated and coefficients on different scales are uncorrelated for any wavelet basis [Wornell and Oppenheim, 1992]. Therefore, at each scale $j = 1..J$, the wavelet coefficients of the discrete wavelet transform can be regarded as independent identically distributed Gaussian variables with zero mean and variance σ_j^2 . For monofractal signals, $\log(\sigma_j^2)$ is a linear function of j [Maxim et al., 2005; Ninness, 1998] and an estimate of the Hurst exponent, H , is obtained by regression of the log-variance of the wavelet coefficients on scale (Fig. 1c).

Multifractal Singularity Spectrum

There are many physical systems that have behaviour too complex to be adequately described by a single scaling exponent. Instead, these multifractal processes, such as turbulent fluid flow, are more completely described by a set of scaling exponents each of which describes the local power law scaling of the process in the immediate neighbourhood of a given point, x . In the case of a turbulent process, where $\varepsilon_r(x)$ denotes the local dissipation of energy within a radius r of x , we have:

$$\varepsilon_r(x) \propto r^{h(x)} \quad (2)$$

where the exponent of this local power law, $h(x)$, is also known as the singularity or Hölder exponent.

The singularity exponents for each point in the process can be grouped into one of a number of singularity components each of which comprises all points with equivalent singularity exponents and has a fractal support with dimension $D(h)$. The plot of $D(h)$ versus h for all singularity components, also known as the singularity spectrum, represents a complete statistical description of a multifractal process.

Many of the methods available to estimate the singularity spectrum of a multifractal process use wavelets to decompose the total energy of the system into a hierarchy of scales. Here, we will use the wavelet transform modulus maxima (WTMM) method [Goldberger et al., 2000; Muzy et al., 1993; Turiel et al., 2006], which is summarised by the following algorithm:

1. Take the continuous wavelet transform of the signal (Fig. 2a) using the second derivative of the Gaussian function as the wavelet basis, generating a set of

Figure 2.

Multifractal analysis of endogenous fMRI oscillations. (a) An illustrative fMRI time-series, with time measured in images, and $TR = 1.1$ s; (b) its continuous wavelet transform represented in time-frequency space as a scalogram; (c) the skeletal curves linking the modulus maxima of the wavelet transform; (d) a plot of the self-similarity exponents of order q , $\tau(q)$ versus q ; (e) the singularity spectrum, $D(h)$ versus h , and its parameterisation by $h_{\max}$ and the ratio $W = W+/W-$ with $W+ =$ half-width half-maximum (HWHM) for $h > h_{\max}$ and $W- =$ HWHM for $h < h_{\max}$.

wavelet coefficients $\{w_{k,j}\}$ each uniquely defined by its location (or time, $k = 1, 2, 3, \dots, K$) and scale ($j = 1, 2, 3, \dots, J$), where larger scales conventionally correspond to lower frequencies (Fig. 2b).

2. Take the absolute value of the wavelet coefficients and connect the local maxima in scale $j + 1$ to proximally located maxima in the immediately smaller scale j . This reduces the scalogram to a set of M connected curves that track maxima across scales. The local maxima are subsequently replaced by their supremum value over all scales connected by the m th ($m = 1, 2, 3, \dots, M$) curve $|w_{\sup}(m)|$; see Figure 2c.
3. The partition function of order q at scale j , $Z(j, q)$, is calculated for each scale of the transform by summing the supremum coefficients for all curves at all scales to the power q , i.e.

$$Z(j, q) \equiv \sum_m |w_{\sup}(m)|^q$$

4. The partition functions are related to the self-similarity exponents of order q by the relation

$$\log Z(j, q) \sim \tau(q) \log j + C(q)$$

meaning that the self-similarity exponents $\tau(q) = qh(q) - 1$ (Fig. 2d) can be estimated by the gradient of a straight line fitted to a double log plot of the partition function $Z(j, q)$ versus scale j , for each q .

5. Finally the singularity spectrum $D(h)$ (Fig. 2e) is obtained by the Legendre transform of the singularity exponents:

$$D(h) = qh(q) - \tau(q) \quad \text{where} \quad h(q) \equiv \frac{d\tau(q)}{dq}$$

Applying this analysis to an illustrative functional MRI time-series (see Fig. 2), the singularity spectrum has a maximum when $h_{\max} \sim 0.5$ and $D(h_{\max}) \sim 0.9$. It is noticeable that there is fractal support for singularity compo-

nents over a wide range of local scaling behaviours, $0.2 < h < 1.2$, indicating that the time-series has multifractal structure.

Functional MRI Experiments: Acquisition and Analysis

Both functional MRI experiments involved healthy participants who had provided informed consent in writing. All scanning was conducted using a MedSpec S300 scanner (Bruker Medical, Ettlingen, Germany) operating at 3.0 T in the Wolfson Brain Imaging Centre, Cambridge, UK. The experiments were approved by the Addenbrooke's NHS Trust Local Research Ethics Committee.

Data were processed with the Camba software library (Brain Mapping Unit, University of Cambridge, UK: <http://www-bmu.psychiatry.cam.ac.uk/software/>).

Effects of Tissue Type and Echo Time on the Hurst Exponent

One hundred and thirty-six 3D gradient-echo echoplanar imaging (EPI) volumes were acquired from 11 healthy participants (7 male, 4 female; aged 22–56 years, mean $\pm$ standard deviation = 35 ± 10 years) with the following parameters held constant: repetition time (TR) = 1,100 ms; image matrix size = $64 \times 64 \times 21$; voxel dimensions = $3.125 \times 3.125 \times 5.000 \text{ mm}^3$. Within a single scanning session, each participant was scanned five times with echo times (TE) = 22.5, 40, 60, 80 and 100 ms. During each 2 m 30 s period of scanning, participants were instructed to lie quietly in the scanner with their eyes closed but not to fall asleep. The order of scanning was counterbalanced for TE over all participants. The first eight images were discarded to allow for T1 saturation effects, leaving 128 volumes available for estimation of the Hurst exponent.

Temporal and spatial motion correction algorithms were initially applied to individual 3D EPI volumes [Bullmore et al., 1996; Suckling et al., 2006] before maps of H and σ^2 were computed in acquisition space and registered into a standard stereotaxic space by an affine mapping. At each intracerebral voxel in standard space, median H was computed across the group for each TE value; and the value of TE at which H and σ^2 were maximal was also identified.

To obtain regions of interest (ROIs) sampling grey and white matter, one axial slice ($z = +28 \text{ mm}$) of the corresponding tissue probability maps in the Montreal Neurological Institute (MNI) standard space [Mazziotta et al., 2001] was selected and thresholded to identify regions with high tissue occupancy, and consequently avoid voxels representing tissue mixtures. Thresholds were adjusted (0.67 for grey matter, 0.73 for white matter) to obtain an adequate sample ($>1,000$) of voxels and so that the ROIs were almost exactly the same size (1,060 voxels for grey matter, 1,062 voxels for white matter) to ensure balance in subsequent statistical testing of H and σ^2 . The median value across participants at each voxel was obtained and

entered into a repeated measures ANOVA to assess the main effects of tissue and TE and a tissue $\times$ TE interaction.

Cognitive Correlates of Long-Memory Parameters in Resting Data

In this experiment, healthy volunteers first performed a fame decision/facial encoding task during fMRI acquisition. Then they were scanned again, about 30 minutes later, while lying quietly in the scanner at rest. The purpose of this design was to investigate possible associations between behavioural performance on the fame decision task and long-memory properties of the subsequently acquired resting data; and to relate the anatomy of such associations to the functional anatomy of the systems activated by the task.

A group of 11 different healthy participants (5 male, 6 female; aged 20–25 years, mean $\pm$ standard deviation (SD) = 22.36 ± 1.86 years) were studied. During the task, a set of visual stimuli were presented (4 s per stimulus) comprising 40 famous faces, 40 unfamiliar faces and 40 fixation crosses in a randomised order; see Bernard et al. [2004] for task details. Participants were instructed to press one of two response buttons to indicate whether a face was famous or not; to press either button at each presentation of the fixation cross; and to try to memorise the faces so that they would recognise them in a subsequent recognition task. Over the course of 8 m 15 s, 450 EPI data volumes were acquired with the following parameters: TR = 1,100 ms; TE = 30 ms; image matrix size = $64 \times 64 \times 21$; voxel dimensions = $3.75 \times 3.75 \times 4.00 \text{ mm}^3$. The first six volumes were discarded to avoid T1 equilibration effects, leaving 444 volumes available for activation mapping (described below).

Twenty-five to thirty-five minutes after completion of the fame decision task, participants were scanned again in a no-task or resting state (eyes closed) for 9 m 36 s, while 524 EPI data volumes were acquired (with parameters identical to the fame decision task); the first 12 volumes were subsequently discarded leaving 512 images available for fractal analysis.

The analysis of the data acquired during the task focused on identification of brain regions that were significantly activated or deactivated by the experimental contrast between correctly-identified famous and non-famous facial encoding trials. A general linear model, with a design matrix created by convolution of the experimental contrast with a model of the hemodynamic response function [Glover, 1999], was regressed onto the pre-processed time series at each voxel [Bullmore et al., 1996; Suckling et al., 2006]. The resulting F statistic maps were registered in MNI standard space by an affine transformation to the 'EPI' template available in the SPM software library (<http://www.fil.ion.ucl.ac.uk/spm>) and the observed median F statistic—a measure of within-group activation—was tested for statistical significance by a cluster-level

permutation test described in detail elsewhere [Bullmore et al., 1999, 2001; Suckling and Bullmore, 2004; Suckling et al., 2006]. Briefly, maps of median F statistics under the null-hypothesis of no task activation were estimated from time-series following wavelet permutation [Bullmore et al., 2001] and mapped into standard MNI space. Probabilistic thresholding was performed in two-stages: First at the voxel-level, all values at all intracerebral voxels from the permuted response maps were pooled to sample the null-distribution. Voxels with values less than the critical value at $P < 0.05$ were set to zero, whilst those exceeding the critical value were shrunk towards zero by subtracting the critical value. This procedure resulted in sets of three-dimensional voxel clusters in the observed and permuted response maps. Cluster-level statistics were then computed as the sum of suprathreshold voxel statistics for all clusters in all maps. Statistical thresholding at the cluster-level proceeded by pooling cluster statistics from permuted response maps to sample the appropriate null-distribution. Critical values for cluster-level statistics were calculated such that the number of type I errors expected under the null-hypothesis < 1 , corresponding to two-tailed $P < 0.005$.

Estimation of H from pre-processed resting data was done for all individual datasets. These maps of H were then registered to MNI standard space by affine transformation. At each intracerebral voxel, a general linear model was used to test the hypothesis that inter-subject variability in H was significantly associated with variability in reaction time for the famous versus non-famous decisions entailed by performing the facial encoding task. The mean reaction time for each participant was regressed on H at each intracerebral voxel. The standardised coefficient associated with reaction time was statistically thresholded by a cluster-wise permutation test, as described above, permuting reaction times to generate surrogate data under the null-hypothesis. As previously, critical values for cluster-level statistics were calculated such that the number of type I errors expected under the null-hypothesis < 1 , corresponding to two-tailed $P < 0.005$.

To explore the fractal dynamics in greater detail, regional singularity spectra were estimated for the time series extracted from each brain region, for each individual, where H was significantly associated with behavioural latency on the preceding fame decision task. The singularity spectra were parameterised by the value of h at which $D(h)$ was a maximum, $h_{\max}$, and the ratio, $W = W+/W-$ of the half-width at half-maximum (HWHM) for the side of the spectrum with $h < h_{\max}$, $W-$, and the HWHM for the side of the spectrum with $h > h_{\max}$, $W+$ (Fig. 2e).

RESULTS

Effects of Tissue Type and Echo Time on the Hurst Exponent

Group maps of the Hurst exponent (median of 11 participants) are shown for representative midcerebral slices at

various echo times in the range $TE = 22.5$ – 100 ms (Fig. 3a). It is clear that H is generally greater than 0.5 , i.e., functional MRI time-series are typically long-memory or persistent processes, and H is generally higher in cortical and subcortical grey matter regions than in central white matter or lateral ventricles. The anatomical distribution of the variance σ^2 has the highest values in the lateral ventricles and sulcal CSF spaces, intermediate values in grey matter and lowest values in white matter (Fig. 3b). Maximum values of H in grey matter regions were generally observed in data acquired with intermediate echo times ($TE = 40$ or 60 ms) (Fig. 3c).

The effects of tissue type and echo time are also summarised at a regional level by the box-plots in Figure 3d,e, which show that both H and σ^2 are greater in grey than white matter regardless of echo time, but greatest in grey matter when $TE = 60$ ms. Analysis of variance confirmed that the main effect of tissue (grey or white matter) was significant for both H [$F(1, 2,129) = 1907.10$, $P \ll 0.001$] and σ^2 [$F(1, 2,129) = 1,599.95$, $P \ll 0.001$]; the effect of echo time was also significant for both H [$F(4, 8516) = 1860.97$, $P \ll 0.001$] and σ^2 [$F(4, 8516) = 1648.22$, $P \ll 0.001$]; and there was a significant interaction between tissue type and echo time for H ($F(4, 8516) = 73.00$, $P \ll 0.001$) and σ^2 ($F(4, 8516) = 310.25$, $P \ll 0.001$). Post-hoc tests showed that H was higher in grey matter than white matter at all values of TE ($t = 36.94, 37.39, 40.99, 31.08, 24.45$ for $TE = 22.5, 40, 60, 80$ and 100 ms, respectively; $df = 2129$, $P \ll 0.001$).

Cognitive Correlates of Long-Memory Parameters in Resting Data

The mean accuracy for recognition of famous faces was 0.82 (SD 0.17 ; range 0.40 – 1.00) with mean reaction time 1.048 (SD 0.258 ; range 0.78 – 1.74) s, and for rejecting non-famous faces mean accuracy was 0.95 (SD 0.06 ; range 0.825 – 1.00) with mean reaction time 1.187 (SD 0.256 ; range 0.70 – 1.65) seconds. There were no significant differences in accuracy ($t(df = 10) = 2.136$, $P = 0.058$) or latency ($t(df = 10) = 1.621$, $P = 0.136$) of response to famous versus non-famous trials. Accuracy and reaction time were significantly correlated ($r = -0.427$; $P = 0.047$) such that faster response was associated with less accurate performance.

Brain regions activated by the contrast between successfully recognised famous face trials and cross-hair fixation included bilateral cerebellum, primary visual cortex, hippocampus, fusiform and lingual gyri, as well as medial frontal gyrus and a region of right inferior and middle frontal gyrus located at MNI coordinates: $x = -40$ mm, $y = 22$ mm, $z = 2$ mm; see Figure 4a. This pattern of activation closely resembles that previously reported from similar paradigms [Bernard et al., 2004; Ishai et al., 2002, 2005]. Brain regions deactivated by the same contrast included regions of anterior and posterior cingulate gyri,

Figure 3. Anatomical and BOLD effects on monofractal dynamics. (a) Brain maps of the Hurst exponent estimated for each resting fMRI time series. Coronal (top, R = right, L = left), sagittal (centre, A = anterior, P = posterior) and axial (bottom) slices through the origin of the MNI standard space are shown; (b) brain maps of the variance of resting fMRI time-series, slice orientations and locations as above; (c) maps representing the echo time (TE) associated with maximum value of the Hurst exponent (left) and signal variance (right), slice orientations and locations as above; (d) boxplots of the regional mean Hurst exponent for grey matter (shaded boxes) and white matter (open boxes) as a function of TE; and (e) boxplots of the regional mean variance for grey matter and white matter as a function of TE. Boxes extend from first to third quartiles, with the median (second quartile) denoted by the horizontal bar and indentation of the box. Vertical dashed lines extend to the data-point closest to (but not greater than) 1.5 times the inter-quartile range beyond the first and third quartiles. Data beyond this range are individually denoted by a cross.

bilateral temporal and parietal cortex previously described as components of a default mode network [Greicius et al., 2003; Gusnard and Raichle, 2001].

Turning to the resting state data, right inferior frontal cortex was the only brain region where there was a significant linear association between inter-subject variability in

Figure 4.

Behavioural correlates of monofractal and multifractal endogenous dynamics. (a) Brain regions activated (yellow) and deactivated (blue) by the contrast between fame decision/facial encoding trials and crosshair fixation. The colours indicate the range of voxel F values above the critical threshold for voxels; (b) right middle and inferior frontal region where variability in the Hurst exponent of resting state data was significantly associated ($P < 0.005$, cluster level) with mean reaction time during the fame

decision task (cross-hairs are centred on $x = -40$ mm, $y = 22$ mm, $z = 2$ mm in MNI standard space); (c) scatterplot of right prefrontal regional mean Hurst exponent versus mean task reaction time for all 11 subjects and the regression (solid) line; (d) regional singularity spectra of the right prefrontal time-series for the two participants with the fastest (0.82 s) and slowest (1.55 s) mean reaction times.

response latency to successfully encoded famous face trials and variability in the Hurst exponent. This locus of association between cognitive task performance and subsequent resting state dynamics was anatomically coincident with the right inferior and middle frontal region activated by

task performance; see Figure 4b. Greater persistence of long-memory dynamics (larger H) in this region was associated with faster response times for the fame decision task performed about 30 minutes before resting state data acquisition; see Figure 4c.

Multifractal analysis was used to compute the regional singularity spectra for the fMRI time series extracted from this right inferior frontal region. The parameters of the singularity spectra, $h_{\max}$ and W , were the dependent variables in a multivariate GLM with response latency as the independent variable. By this analysis, there was a significant association between multifractal dynamics and response latency ($F(2,8) = 5.849$; $P = 0.027$), although the corresponding univariate tests were not significant. For illustration, singularity spectra from participants with the fastest (820 ms) and slowest (1,550 ms) mean reaction times to the fame decision task are shown in Figure 4d. The maximum of the singularity spectrum was shifted to a higher value of h and the asymmetric dispersion of the spectrum was greater in the fast-responding participant. These observations of h are compatible with the observation that the Hurst exponent H is greater in the fast-responding participant and indicate that a relative increase in H can represent a change in multifractal dynamics.

DISCUSSION

Low frequency endogenous oscillations and correlations have been frequently recognised since the advent of functional magnetic resonance imaging in the mid-1990s, yet have also often been regarded as awkward, anomalous or possibly artefactual.

Awkward in the sense that the existence of long-memory or $1/f$ -like “coloured noise” in fMRI initially complicated efficient estimation of general linear models of brain activation experiments. Although this problem has been substantially resolved by widespread adoption of autoregressive models for GLM residuals [Bullmore et al., 2001; Friston et al., 2000; Woolrich et al., 2001], it may have left a misleading impression that endogenous processes are troublesome noise substantively as well as statistically.

Anomalous because fMRI dynamics are necessarily limited to a very low frequency range, about 0.01–0.1 Hz, which had not been of mainstream interest to prior EEG or MEG studies considering the frequency range 1–100 Hz. This has made it difficult to cross-validate resting state networks observed in fMRI by comparison to systems measured using neuronal electromagnetic signals with equivalent bandwidth. It is anomalous also in the conceptual framework of most activation experiments, because it is not immediately obvious how such slow dynamics might relate to the much faster dynamics entailed in responding to a single activation trial, lasting say 1–2 s, in an event-related fMRI design, and possibly artefactual because such slow, $1/f$ -like or long-memory dynamics are virtually ubiquitous in diverse physical systems and do not necessarily represent neuronal dynamics; slow background activity in ‘raw’ fMRI time-series certainly includes major contributions from participant movement, respiration, pulsation and instrumental sources [Birn et al., 2006; Cordes et al., 2001].

Here, we have used the concepts and tools of fractals and wavelet analysis to capture more-or-less succinctly the complexity of fMRI time-series and to show how these fractal and multifractal measures are (a) likely engendered by the same neurovascular coupling mechanism that mediates the BOLD activation response to experimental stimulation; and (b) related to cognitive task performance.

Anatomical and BOLD Associations with Monofractal Dynamics

The anatomical distribution of the Hurst exponent broadly delineates the grey-white matter boundary, with values estimated in grey matter representing significantly longer memory. This result is similar to the anatomical maps of H previously reported in groups of healthy elderly participants [Maxim et al., 2005] and in an individual young participant [Shimizu et al., 2004]. Typically $H < 0.85$, which is within the range the algorithm provides unbiased estimates and confirms the utility of this wavelet-based estimator of monofractal dynamics in the context of fMRI [Maxim et al., 2005].

As TE was increased to 100ms, this monofractal contrast between grey and white matter was degraded and there was a strong TE $\times$ tissue interaction. Additionally, both H and signal variance demonstrate a unimodal distribution as a function of TE, with maximum value when TE = 40–60 ms. Echo planar imaging is most sensitive to BOLD when TE $\sim$ T2* for the tissue, which is typically around TE = 50 ms [Chen et al., 2005; Wansapura et al., 1999; Wu and Li, 2005]. In contrast, similar plots for white matter show less pronounced unimodal behaviour as a function of TE and that H is generally smaller than in grey matter, although greater than 0.5.

We have thus provided quantitative evidence for the prior observation [Maxim et al., 2005] that fMRI dynamics are more persistent or long-memory in grey matter regions than white matter or CSF regions, suggesting that persistence could be an indicator of neuronal processing. We have additionally demonstrated for the first time that persistence of grey matter dynamics is greatest in data acquired with echo times that approximate the T2* decay constant and are therefore optimised to detect BOLD contrast. This observation is compatible with the view that fractal properties of the resting state fMRI signal are produced by the same neurovascular coupling that mediates the activation response to experimental stimulation. On the contrary, it suggests that resting state dynamics are not driven by systemic changes in flow or volume.

Behavioural Correlates of Monofractal and Multifractal Endogenous Dynamics

The relationship between low frequency endogenous oscillations and cognitive performance was addressed experimentally by correlating a monofractal measure—the Hurst exponent—for resting state time series with the

latency of correct decision making in an activation experiment conducted about 30 minutes before the resting state data were acquired. This disclosed an area of right inferior and middle frontal cortex, where faster decision-making was significantly correlated with greater persistence of endogenous oscillations measured subsequently. This region was anatomically embedded in the larger system activated by the task, additionally supporting the functional relevance of the statistical association.

We also explored the multifractal properties of endogenous oscillations recorded from this region of right prefrontal cortex. As exemplified by the broad range of the singularity spectra, there was strong and consistent evidence that multifractal analysis is appropriate to the complexity of these data. Furthermore, the multivariate parameters of the spectra were significantly associated with task performance: faster responders had more positively skewed spectra and larger maximum singularity exponents, indicating local scaling behaviours that extend further over time.

Many prior biofractal studies—in electrocardiography as well as EEG and fMRI—have shown that greater or abnormal persistence of monofractal dynamics is often a marker of pathophysiological deterioration, whether by normal ageing, dementia, or heart failure [Goldberger et al., 2002; Ivanov et al., 1999; Maxim et al., 2005], whereas, in this data, we have shown that greater persistence can be related to faster behavioural performance. However, it is notable that in this case faster does not mean better—faster reaction time was negatively correlated with performance accuracy—suggesting that greater persistence in brain fractal dynamics, as in other biofractal processes, might be a marker of less than optimal function.

A major limitation of this experiment is that it cannot resolve the directionality of effects that might underlie this association between task performance and endogenous oscillations. Are changes in the fractal dynamics of activated frontal regions a delayed effect of faster task performance, or might it somehow have supported or predisposed to faster performance? Both hypotheses remain tenable. Our results merely refute the general null hypothesis that endogenous fMRI dynamics are irrelevant to an understanding of cognitive function. The more detailed investigation of such associations, including elucidation of the causal relations between cognitive function and endogenous fMRI dynamics must await further experiments.

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