
A WAVELET-BASED FRAMEWORK FOR MAPPING LONG MEMORY IN RESTING-STATE fMRI: AGE-RELATED CHANGES IN THE HIPPOCAMPUS FROM THE ADHD-200 DATASET

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ABSTRACT

Functional magnetic resonance imaging (fMRI) time series are known to exhibit long-range temporal dependencies that challenge traditional modeling approaches. In this study, we propose a novel computational pipeline to characterize and interpret these dependencies using a long-memory (LM) framework, which captures the slow, power-law decay of autocorrelation in resting-state fMRI (rs-fMRI) signals. The pipeline involves voxelwise estimation of LM parameters via a wavelet-based Bayesian method, yielding spatial maps that reflect temporal dependence across the brain. These maps are then projected onto a lower-dimensional space via a composite basis and are then related to individual-level covariates through group-level regression. We applied this approach to the ADHD-200 dataset and found significant positive associations between age in children and the LM parameter in the hippocampus, after adjusting for ADHD symptom severity and medication status. These findings complement prior neuroimaging work by linking long-range temporal dependence to developmental changes in memory-related brain regions. Overall, the proposed methodology enables detailed mapping of intrinsic temporal dynamics in rs-fMRI and offers new insights into the relationship between functional signal memory and brain development.

Keywords Attention-Deficit/Hyperactivity Disorder · Bayesian inference · Long-Memory Processes · rs-fMRI, ADHD 200

1 Introduction

Functional Magnetic Resonance Imaging (fMRI) is a non-invasive neuroimaging technique that measures brain activity by detecting changes in blood oxygenation levels over time. This relies on the Blood Oxygen Level Dependent (BOLD) signal [Ogawa et al., 1990], which reflects local changes in the balance between oxygenated and deoxygenated hemoglobin following neural activation, providing an indirect measure of brain activity. Resting-state fMRI (rs-fMRI) enables the study of intrinsic functional networks without task-based stimuli and is widely used in both basic and clinical neuroscience [Bijsterbosch et al., 2017]. In this study, we propose a novel voxelwise Bayesian framework to estimate long-memory properties of rs-fMRI time series and examine their associations with individual-level clinical

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covariates. We demonstrate the approach using the ADHD-200 preprocessed dataset [Bellec et al., 2017], which includes resting-state scans and behavioral measures from children and adolescents.

While most resting-state fMRI studies focus on spatial patterns of functional connectivity, less attention has been given to the temporal structure of the BOLD signal itself. In this work, we investigate whether the long-memory (LM) parameter offers a meaningful way to characterize intrinsic brain activity and relate it to covariates of interest. Accurately modeling temporal dependencies is essential for analyzing rs-fMRI data. While traditional autoregressive (AR) models have been widely used [Woolrich et al., 2001, Lenoski et al., 2008], they assume short-range memory and may not fully capture the rich temporal organization of the BOLD signal, which has been shown to exhibit dependencies extending several minutes into the past [Tagliazucchi et al., 2013]. Our framework explicitly models these long-range dependencies using a long-memory process. Previous studies [Zarahn et al., 1997, Aguirre et al., 1997] accounted for long-range effects through correlated noise in regression models, whereas we model each voxel’s signal as a long-memory process and use spatial regression to relate these estimates to subject-level covariates [Sokunbi et al., 2014]. This approach allows us to explore complex temporal dynamics that may reflect underlying neural processes beyond what is captured by traditional connectivity-based analyses.

The nonlinear and scale-free nature of fMRI signals has been explored in numerous studies [Bullmore et al., 2004, Vazquez and Noll, 1998, Birn et al., 2001, Bullmore et al., 2001, Xie et al., 2008]. Although long-memory models are not explicitly nonlinear, they capture temporal complexity that reflects persistent, scale-invariant patterns in the BOLD signal—features that are often associated with nonlinear or fractal behavior in neuroimaging data. In our framework, we model fMRI time series at each voxel as long-memory processes, which results in dense covariance structures. To address the resulting computational burden, we apply the discrete wavelet transform (DWT) [Mallat, 1989], which transforms the data from the time domain to the time-frequency domain, yielding a near-diagonal covariance structure with power-law decay [Fadili and Bullmore, 2002, Meyer, 2003, Jeong et al., 2013, Maxim et al., 2005]. This transformation facilitates efficient estimation of long-memory parameters and enables the analysis of brain signal dynamics across multiple temporal scales.

A variety of methods have been proposed to analyze the dynamics of fMRI time series. These include connectivity-based approaches such as time-resolved graph theory [Maffei and Sessa, 2021] and dynamic functional connectivity measures [Pedersen et al., 2017], which examine how functional connections between brain regions fluctuate over time. Entropy-based methods evaluate the temporal complexity of fMRI signals by quantifying the degree of signal unpredictability or irregularity, and are often used to assess neural efficiency, cognitive state, or disease-related disruptions [Omidvarnia et al., 2022, McDonough and Nashiro, 2014, Nezafati et al., 2020]. In contrast, our work adopts a long-memory modeling approach as a distinct spatiotemporal framework for examining brain temporal complexity through power-law scaling behavior [La Rocca et al., 2018]. We characterize this behavior using the long-memory parameter, which quantifies the persistence (or anti-persistence) of fluctuations in time series data and is linearly related to the Hurst exponent (H)—a widely used measure in the fractal analysis of fMRI signals [Wu et al., 2010, Vyushin and Kushner, 2009, Dong et al., 2018, Akhrif et al., 2018, Campbell et al., 2022]. We extend this modeling to the spatial domain by employing a Bayesian spatial regression framework, enabling voxelwise estimation of long-memory parameters and their relationships with covariates. This spatially informed approach allows us to characterize latent brain dynamics beyond what is captured by connectivity or entropy-based methods.

Long-range dependence, often observed in complex dynamical systems, manifests as scale-free behavior across physical, biological, and social domains [Bak et al., 1987]. BOLD fMRI signals exhibit similar scale-free properties [Ciuciu et al., 2012], where the power spectral density (PSD) of the signal follows a power-law decay. Scale-free properties refer to the absence of a characteristic time scale in the signal’s dynamics, meaning that statistical patterns—such as the distribution of spectral power—remain consistent across temporal scales. A linear relationship in log-log plots of the PSD indicates a power-law distribution of spectral power, which reflects scale-free, long-range temporal correlations in the signal. Recent studies [Omidvarnia et al., 2022, Medel et al., 2023] have demonstrated consistent associations between brain temporal complexity and the slope of the PSD in log-log space, which is directly related to the long-memory parameter. Consequently, resting-state fMRI signals exhibit long-memory behavior across various brain regions, reflecting intrinsic long-range temporal dependencies in neuronal activity [Lahmiri, 2018, Campbell and Weber, 2022]. Investigating these properties is essential for understanding the brain’s temporal complexity and the mechanisms underlying its functional organization in both health and disease.

We model the autocovariance structure of the fMRI signal at each voxel v using a long-memory process defined by $[\Sigma_v]_{ij} = \gamma(|i - j|)$, i and j being temporal coordinates, and $\gamma(h) \propto h^{-\alpha}$ for large lag values h . The parameter α characterizes the rate of decay and is referred to as the long-memory parameter. This formulation stands in contrast to the commonly assumed autoregressive model of order one (AR(1)), $\gamma(h) \propto \rho^h$, which captures only short-range dependencies and may be inadequate for modeling the persistent correlations observed in resting-state fMRI signals. To analyze these long-range dependencies more effectively, we employ the Discrete Wavelet Transform (DWT), which

transforms the fMRI signals into the time-frequency domain. This yields a diagonal covariance matrix Σ_v^* , whose entries vary with scale and take the form $\Sigma_v^* = \nu \cdot \text{diag}(2^{-\alpha_v m})$, where m indexes the wavelet scale. This representation provides a more tractable and accurate framework for estimating voxelwise long-memory parameters.

The value of α is estimated for each voxel and theoretically ranges between 0 and 1. In our framework, all values of α represent long memory behavior. Values of α closer to 0 correspond to stronger long memory reflecting highly persistent correlations over time, whereas values of α closer to 1 indicate weaker long memory, corresponding to more rapid decay of autocorrelation. An α value approaching 1 corresponds to the boundary of white noise behavior, i.e., uncorrelated fluctuations. Accurate estimation of the long-memory parameter α is crucial for capturing the underlying temporal dynamics of fMRI signals and relating them to clinical or developmental covariates. To achieve this, we employ Bayesian inference in conjunction with the DWT, which provides both computational efficiency and a probabilistic framework for incorporating prior information and quantifying uncertainty in voxelwise estimates.

There are multiple approaches in the literature for estimating the long-memory parameter. Heuristic and graphical methods, such as the R/S method and Detrended Fluctuation Analysis (DFA), offer straightforward computation of scaling exponents but may be sensitive to noise or limited time series length in practical applications [Lo, 1991, Peng et al., 1994]. Bayesian inference, by contrast, provides a probabilistic framework for incorporating prior knowledge and modeling uncertainty in the estimation of long-memory parameters [Holan et al., 2009, Graves et al., 2014, Jeong et al., 2013, Zhang et al., 2014]. A major computational challenge in this setting arises from the estimation of high-dimensional and dense covariance matrices in voxelwise fMRI data. To address this, we employ the Discrete Wavelet Transform (DWT), which decomposes the data into multiple scales and transforms the covariance structure into a near-diagonal form [Fadili and Bullmore, 2002], thereby substantially reducing computational burden. Following [Jeong et al., 2013], we use the variance progression formula [Wornell, 1993, Vannucci et al., 1998], which models how the variance of wavelet coefficients changes across scales m , and directly informs the diagonal structure of Σ_v^* used to estimate the long-memory parameter. This approach accommodates a wide range of long-memory processes and supports the analysis of brain dynamics across different time scales and frequency bands. By estimating the long-memory parameter embedded in the wavelet coefficients, we are able to investigate scaling properties and relate them to underlying neural mechanisms.

Our study makes several key contributions to the field of neuroimaging data analysis. First, we introduce a novel Bayesian spatial modeling approach for estimating long-memory parameters, which addresses the computational challenges posed by high-dimensional covariance structures in voxelwise fMRI data. Second, our analysis provides a comprehensive investigation of long-memory dynamics in fMRI signals, exploring their associations with individual-level covariates. Finally, we identify significant relationships between the long-memory parameter and the age of children and adolescents in the Hippocampus and anterior lobe regions. These findings contribute to the growing body of evidence linking brain temporal complexity to developmental changes in functional brain organization.

The paper is organized as follows. Section 2 outlines the main contribution of this article, our novel methodological approach, including the estimation of individual long-memory maps in Subsection 2.1 and the subsequent multi-subject analysis and dimension reduction in Subsection 2.2, which investigate associations between long-memory parameters and selected covariates. In Section 3 we apply our proposed neuroimaging analysis framework to the ADHD 200 data and presents the results of this analysis, summarizing the estimated long-memory maps and identifying subject characteristics associated with the long-memory parameter. Finally, Section 4 discusses the implications of these findings, highlights study limitations, and proposes directions for future research.

2 Methods

Our proposed pipeline consists of two main stages. In the first stage, we perform a subject-level analysis to estimate long-memory parameters at each voxel. Without loss of generality, we assume that the BOLD time series at each voxel is centered at zero, and model it as a mean-zero Gaussian process with covariance matrix Σ_v , characterized by a power-law decay. We apply the Discrete Wavelet Transform (DWT) to each voxelwise time series, which transforms the covariance Σ_v into a near-diagonal matrix Σ_v^* , whose structure is governed by two parameters: the long-memory parameter α_v and the innovation variance σ_v^2 . This transformation enables efficient estimation of α_v and σ_v^2 . A Bayesian Markov Chain Monte Carlo (MCMC) method is used to obtain posterior distributions of these parameters at each voxel and for each subject, yielding subject-specific spatial maps of long-memory characteristics.

After estimating the long-memory parameter maps for each subject, we proceed to the second stage of the analysis, which aims to relate these spatial maps to covariates of interest (e.g., clinical scores or demographic variables). Each subject's estimated $\alpha_i = \{\alpha_{iv}; v = 1, \dots, N_v\}$ map serves as an imaging phenotype, capturing the spatial distribution of temporal dependencies across the brain. To address the challenges of high dimensionality and spatial correlations, we implement a composite-basis approach. This method uses singular value decomposition (SVD) on local features

within a parcellated spatial space and subsequently captures global spatial patterns. The dimension-reduced spatial features obtained from the composite-basis projection are then used in a group-level Bayesian regression analysis to assess how long-memory properties vary with individual characteristics.

2.1 Subject-level analysis

At the subject level, we estimate long-memory parameters independently for each voxel time series. Let $\mathbf{Y}_v = (Y_{v1}, \dots, Y_{vT})^\top$ denote the BOLD signal vector at voxel v with T time points. Assuming the data have been centered, we model \mathbf{Y}_v as a realization from a zero-mean Gaussian process with covariance matrix Σ_v , which reflects the temporal dependence structure at that voxel. To account for this temporal dependence, we model each time series as a long-memory process. These signals exhibit a complex structure characterized by dependencies across multiple time scales.

Figure 1 illustrates the characteristic long-memory behavior of a single fMRI time series from our motivating application, shown in both the temporal and spectral domains. Panel (a) presents a time series of fMRI data acquired from a single voxel, measuring the intensity of the BOLD signal at each time point. Panel (b) depicts the power spectral density (PSD) of this signal for frequencies below 0.5 Hz. The presence of peaks in the PSD indicates dominant frequency components below 0.15 Hz. In panel (c), the log-log plot of spectral density versus frequency shows a flat line over the interval $[-3, -0.8]$, characteristic of white noise behavior. Over the interval $[-0.8, -0.1]$, we observe an approximately linear relationship, which indicates the presence of long-range dependencies in the data. This linear behavior in the log-log plot is a signature of a long-memory process, with the slope — often referred to as the spectral exponent — directly related to the long-memory parameter [Clauset et al., 2009].

A flat log spectral density in the lower log-frequency range implies that the fMRI signal behaves like white noise, whereas the presence of dominant low-frequency components and linearity at higher log frequencies suggests power-law behavior. The Discrete Wavelet Transform (DWT) is particularly suited to address the multi-scale nature of the signal, providing a framework to capture long-memory dynamics efficiently across different frequency bands.

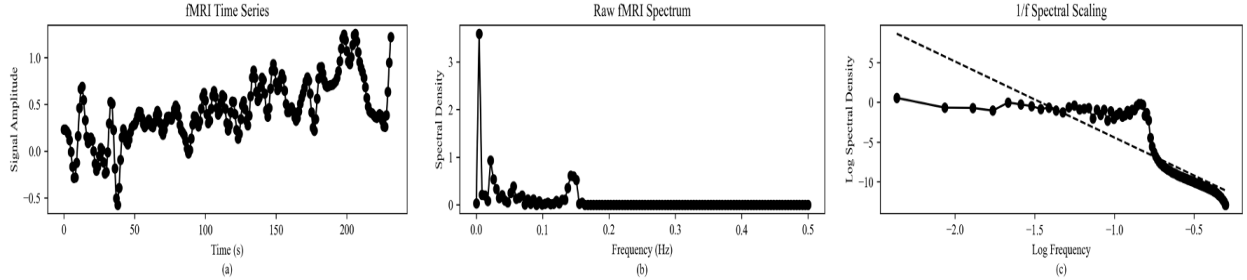


Figure 1: Long-memory behavior of fMRI time series. (a) fMRI time series from a single brain voxel; (b) power spectral density (PSD) of the time series, highlighting dominant low-frequency components; (c) log-log plot of the spectral density, displaying white noise behavior at lower frequencies and long-memory behavior at higher frequencies, characterized by a power-law exponent.

[Vannucci et al., 1998] proposed a method to compute the covariance of wavelet coefficients using the recursive filters of the DWT. We adopt their approach to characterize long-memory processes by modeling the covariance structure of the error process \mathbf{E}_v at each voxel. Specifically, we assume that the covariance matrix $\Sigma_v(i, j)$ is given by $\gamma(|i - j|)$, where $\gamma(h)$ follows a power-law decay:

$$\gamma(h) \propto \frac{1}{h^\alpha}, \quad (1)$$

where h is the lag and α is the long-memory parameter governing the rate of decay of autocorrelations as h increases.

To simplify the dense structure of the autocovariance matrix of the long-memory process, we apply the discrete wavelet transform (DWT) to the processes $\{\mathbf{E}_v, v = 1, \dots, N_v\}$ [Mallat, 1989]. The DWT is based on wavelet basis functions derived from a mother wavelet ψ , defined as

$$\psi_{m,n}(x) = 2^{m/2} \psi(2^m x - n),$$

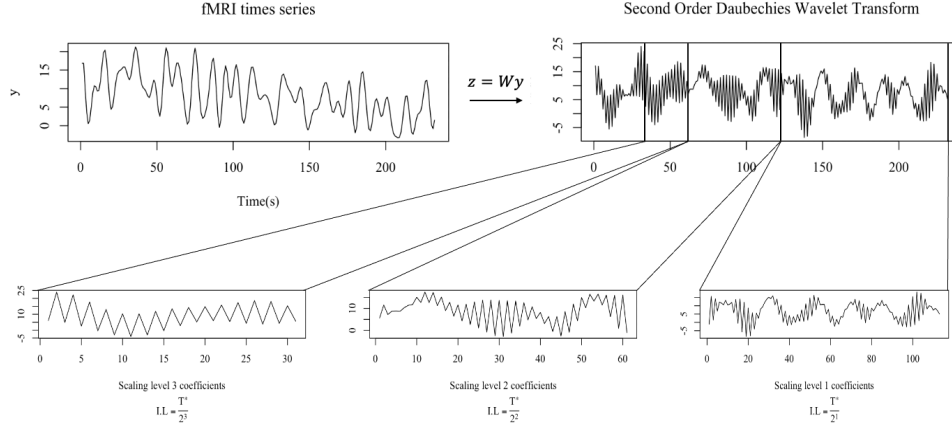


Figure 2: Top left: time series plot of the fMRI BOLD signal in the time domain. Top right: one-dimensional discrete wavelet transform (DWT) of the signal in the frequency domain. Bottom row: zoomed-in plots of the decomposed signal at different scale levels. The interval length (I.L.) is shown for each scale j , defined as $T^*/2^j$, where T^* is the length of the transformed signal.

where m denotes the scale (which controls the frequency band analyzed), and n denotes the translation (which determines the location in time). The DWT projects each time series onto this set of basis functions, yielding

$$Y_v^* = WY_v,$$

where the discrete wavelet transformation matrix W is constructed as follows:

1. **Generate wavelet basis functions:** For each scale level m and each translation n , the wavelet basis function $\psi_{m,n}(x)$ is computed. This results in a collection of wavelet basis functions that together decompose the signal.
2. **Construct the matrix:** The matrix W is constructed by placing each of these discretized wavelet basis functions as rows. Each row w_r corresponds to a discretized version of the wavelet basis function $\psi_{m,n}(x)$. The rows are ordered by scale, from the finest (capturing high-frequency components) to the coarsest (capturing low-frequency components), and are followed by the scaling function coefficients V_m .
3. **Matrix dimensions:** If the original time series contains T time points, then the resulting matrix W has dimensions $T^* \times T$, where T^* depends on the number of wavelet decomposition levels. Each row of W corresponds to a wavelet coefficient associated with a specific scale and time shift, while each column represents the contribution of the original time-domain data to the wavelet coefficients.
4. **Orthogonality:** When orthogonal wavelet basis functions are used, the matrix W is orthogonal, satisfying $W^T W = I$. This property simplifies both the wavelet decomposition (via multiplication by W) and the reconstruction of the original signal (via multiplication by W^T).

When determining the discrete wavelet transformation matrix, the scaling level m must be specified in advance. A higher value of m increases the ability to capture lower-frequency components of the signal. Therefore, m should be carefully selected based on the frequency range of the data. Figure 2 illustrates a second-order Daubechies wavelet decomposition of a single fMRI time series. The transformed signal is separated into components corresponding to different scale levels, each capturing activity at a distinct frequency range. The figure shows both the overall decomposition and zoomed-in views of selected scale-level components.

When the DWT is applied to Y_v , it transforms the covariance matrix from Σ_v to $\Sigma_v^* = W\Sigma_v W^T$. This transformation yields the covariance matrix of the time series Y_v^* in the wavelet domain for each voxel v . The correlation between wavelet coefficients at different scales decreases rapidly [Dijkerman and Mazumdar, 1994, Fan, 2003]. Therefore, it is reasonable to approximate Σ_v^* as a diagonal covariance matrix, with diagonal elements $\nu_v \sigma_{mn}^2$ corresponding to the variance of the n th wavelet coefficient at the m th scale level. We adopt the variance progression formula proposed in [Wornell, 1993, Jeong et al., 2013]:

$$\nu_v \sigma_{mn}^2 = \nu_v (2^{\alpha_v})^{-m}, \quad (2)$$

where ν_v is the innovation variance, $\alpha_v \in (0, 1)$ is the long-memory parameter, and m is the wavelet scale level. Here larger values of m indicate coarser approximations. The long-memory parameter α_v is linearly related to the Hurst exponent H by the equation $\alpha_v = 2 - 2H$ for $1/2 < H < 1$, as established in [Vyushin and Kushner, 2009, Suibkitwanchai, 2022].

We estimate the long-memory parameter $\alpha_v \in (0, 1)$ simultaneously with the innovation variance ν_v using a Bayesian approach, assuming $\alpha_v \sim \text{Beta}(a, b)$ and $\nu_v \sim \text{Inv-Gamma}(p, s)$ *a priori*. The Markov chain Monte Carlo (MCMC) algorithm used to sample from the posterior distribution is described in Appendix 5. Our approach combines a truncated Metropolis–Hastings algorithm to sample from the posterior of α_v with Gibbs sampling for ν_v . This yields posterior distributions of the long-memory parameters across all voxels for each subject.

2.2 Group-level analysis

For subject i , let $\alpha_{i,v}$ denote the long-memory parameter at voxel v , for $i = 1, \dots, N$. Let $\alpha_v = (\alpha_{1,v}, \dots, \alpha_{N,v})^\top$ denote the vector of estimated posterior means of the long-memory parameters at voxel v across all N subjects. We model α_v as a function of subject-specific covariates as follows:

$$\alpha_v = \mathbf{Z}\beta_v + \epsilon_v, \quad (3)$$

where \mathbf{Z} is an $N \times Q$ design matrix. The regression coefficients β_v characterize the relationship between the covariates \mathbf{Z} and the estimated long-memory parameters at voxel v . Collectively, we define $\beta = \{\beta_1, \beta_2, \dots, \beta_{N_v}\}$, representing the regression coefficients across all voxels, for $v = 1, 2, \dots, N_v$.

We apply the composite-basis approach proposed in [Miranda and Morris, 2021] to capture both local and global spatial dependencies across voxels in the regression matrix β , while effectively reducing dimensionality to maintain computational tractability. This strategy is specifically designed to address the spatial structure of the data. The composite-basis approach consists of two steps. First, the brain is divided into biological regions of interest (ROIs). For each ROI, local bases are obtained using singular value decomposition (SVD) of data matrices composed of observations within that ROI. The data are then projected onto these local bases. Second, the projected data are used to derive a second-level basis via SVD applied to the output of the first step. Let α denote an $N \times N_v$ matrix, where each row i contains the long-memory map for subject i across all voxels, i.e., the row vector $(\alpha_{i,1}, \dots, \alpha_{i,N_v})$. We apply the composite-basis approach by rewriting the model in (3) as follows:

$$\alpha\Upsilon = \mathbf{Z}\beta\Upsilon + \epsilon\Upsilon, \quad (4)$$

where $\Upsilon = \Phi\Psi$ denotes the composite basis. The matrix $\Phi = \text{blkdiag}(\Phi_1, \dots, \Phi_{N_{\text{ROI}}})$ is block-diagonal, with each block Φ_r consisting of the orthonormal eigenvectors obtained from the singular value decomposition of the data in the r th ROI. These matrices capture the dominant modes of variability within each ROI. The second-level basis Ψ captures variability across ROIs, based on the projected local features. This approach first projects each ROI into a lower-dimensional space containing local features, and then captures global structure using the basis Ψ , whose columns are orthonormal eigenvectors of the projected data. The resulting composite basis provides regularization and dimensionality reduction by thresholding the number of principal components according to the proportion of explained variability.

Model (4) can be rewritten as

$$\alpha^* = \mathbf{Z}\beta^* + \epsilon^*, \quad (5)$$

where α^* is a $N \times PC_f$ matrix containing the long-memory maps projected into the basis space. The matrix \mathbf{Z} is the $N \times Q$ design matrix containing population-level covariates. For each column of ϵ^* , we assume $\epsilon_r^* \sim N(0, \delta_r^2 \mathbf{I})$, for $r = 1, \dots, PC_f$. The $Q \times PC_f$ coefficient matrix β^* captures the relationship between the long-memory maps and the covariates of interest.

To estimate β^* , we specify the following priors:

$$\begin{aligned} \beta_r^* \mid \delta_r^2 &\sim \text{MVN}(\mu_0, \delta_r^2 \Lambda_0), \\ \delta_r^2 &\sim \text{Inverse-Gamma}(k, l) \end{aligned} \quad (6)$$

Note that the prior for $\beta_{PC_r}^*$ depends on $\delta_{PC_r}^2$. The hyperparameters for the inverse-gamma distribution were set to $(k, l) = (0.1, 0.5)$ to restrict large variances in the regression coefficients. For the multivariate normal distribution, we defined the hyperparameters as $(\mu_0, \Lambda_0) = (\mathbf{0}, 100 \times (\mathbf{Z}^\top \mathbf{Z})^{-1})$, based on the assumption that the estimated values

of β^* would be centered around zero. Estimation of β^* proceeds via MCMC and is described in Appendix 5. After obtaining posterior samples for β^* , we project these samples back into the original voxel space via the inverse of the composite basis, Υ^{-1} . These steps enable voxel-level inference even though the MCMC sampling is done over the lower-dimensional basis space.

3 Results

We analyze data from the ADHD-200 consortium, publicly available through the Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC) and detailed in [Bellec et al., 2017]. This dataset consists of 973 individuals aged 7 to 27 years with preprocessed resting-state functional MRI (rs-fMRI) data, collected from 17 studies across 8 sites. Of these individuals, 352 are female and the remaining are male. The data include phenotypic information alongside rs-fMRI for each participant.

The repository offers data processed through multiple pipelines: Athena, Burner, and NIAK. We selected the Athena pipeline for this study due to its compatibility with our research objectives. The Athena pipeline processed rs-fMRI using a custom BASH script that integrates AFNI [Cox, 1996] and FSL [Smith et al., 2004] neuroimaging toolkits. Each rs-fMRI dataset consists of $49 \times 58 \times 47$ voxels and varies in length from 75 to 234 time points due to different acquisition protocols. Preprocessing steps included removal of the first four volumes, slice-timing correction, and motion correction using realignment. The functional data were then co-registered to the standard MNI152 template space with a resolution of $4 \times 4 \times 4$ mm³. To mitigate physiological noise, head motion artifacts, and scanner drift, nuisance regressors, including signals from white matter, cerebrospinal fluid, and six head motion parameters, were regressed out. Finally, the data were spatially smoothed with a 6 mm FWHM Gaussian kernel.

We analyzed a final sample of 355 participants with complete unfiltered rs-fMRI data and full phenotypic information for key covariates. This subset was selected to ensure the data were suitable for time-frequency analysis at the first level. Phenotypic variables included sex at birth, age, ADHD diagnosis (combined, inattentive, or hyperactive-impulsive), and medication status. ADHD severity was measured using the Conners' Parent Rating Scale-Revised, long version (CPRS-LV) [Conners, 1997], treated as a continuous variable ranging from 19 to 90. Age was also treated as continuous (range: 7–18), while sex at birth and medication status were binary. Previous studies have identified associations between ADHD symptoms and age, sex, and medication status [Ivanov et al., 2014, Yang et al., 2011, Bollmann et al., 2017]. Based on these findings, we selected age, ADHD severity, medication status, and their interaction as primary covariates of interest. Table 1 summarizes the distribution of participants across key subgroups.

	ADHD/MED	ADHD/NO MED	NO ADHD
Male	7	24	101
Female	36	72	115

Table 1: Distribution of participants by sex and ADHD diagnosis. MED: medicated, NO MED: Unmedicated

Our analysis pipeline is summarized in Figure 3. Panel A shows that for each subject i , we first estimate long-memory parameter maps α_v , $v = 1, \dots, N_v$ using the Bayesian approach described in Section 2.1. Panel B shows how these subject-level maps are combined to form a group-level representation of long-memory patterns across the brain. Panel C illustrates how Bayesian inference is then used to examine the effects of covariates on the long-memory parameters in the reduced space as illustrated in part C of Figure 3.

3.1 Subject-level analysis

At the subject level, we estimated the voxelwise covariance matrix Σ_v^* in the wavelet domain, parameterized by the long-memory parameter $\alpha_v \in (0, 1)$ and the innovation variance ν_v , as described in Section 2.1. We assigned a Beta(3, 3) prior to α_v and an inverse-gamma(2, 2) prior to ν_v , with the latter chosen to accommodate large variance values through heavier tails. Estimation was carried out via MCMC sampling, with implementation details provided in Appendix A.

Figure 4 presents the group-averaged long-memory maps for two representative subgroups selected for illustration purposes: participants aged 12 years or older, and those aged 9 years or younger. In the next section, we examine how covariates influence the spatial distribution of long-memory estimates.

3.2 Group-level analysis

We conducted a group-level analysis to examine how long-memory properties of the BOLD signal vary with age, ADHD severity, and medication status. Specifically, we assessed how these covariates relate to spatial patterns in the estimated long-memory parameters across the brain.

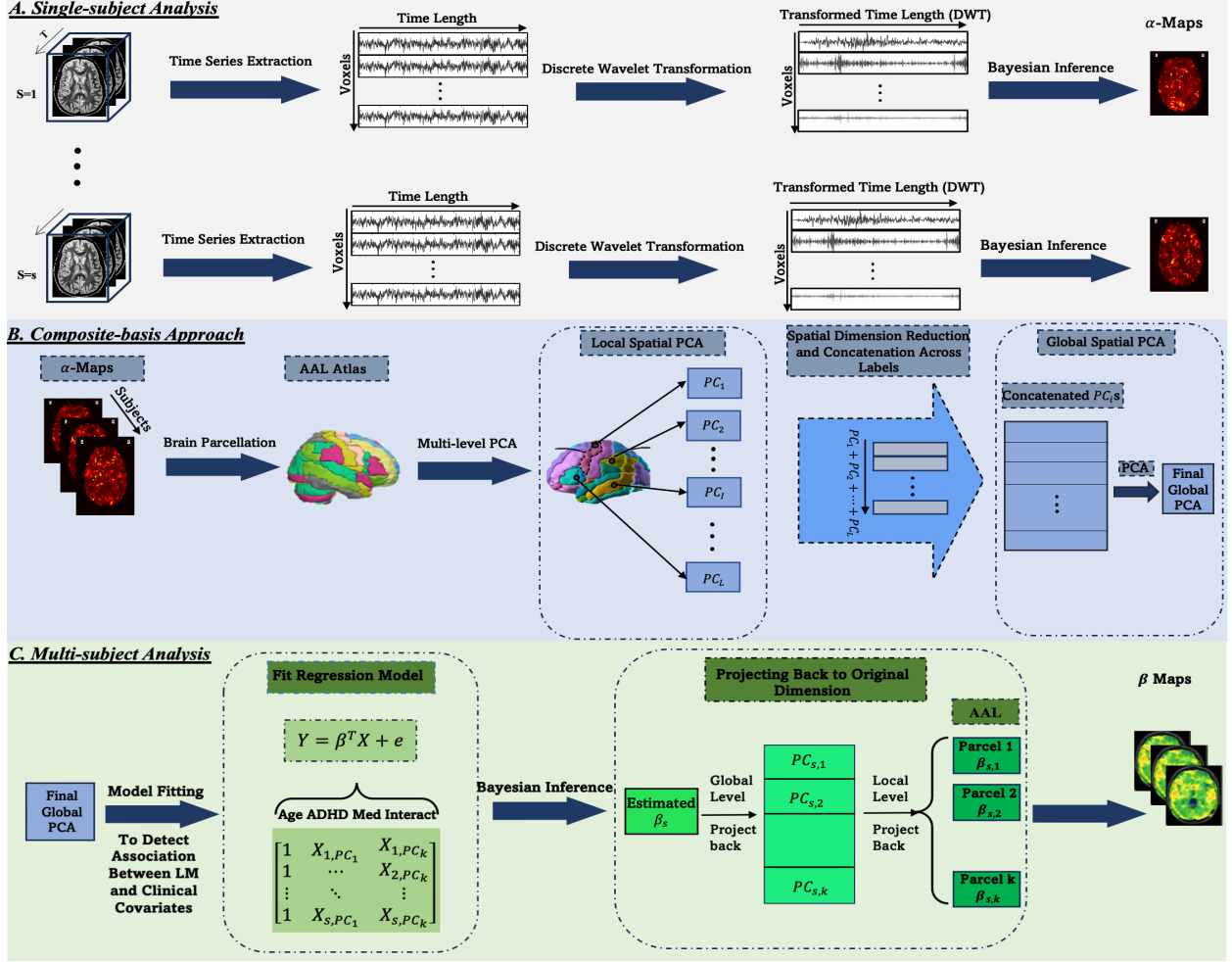


Figure 3: Flowchart of the analysis pipeline. Step A shows the subject-level analysis. First, the Discrete Wavelet Transform is applied to the extracted time series from the 4D fMRI data. Then, long-memory parameters (α -maps) are estimated for each subject using the Bayesian approach. Step B shows the group-level analysis. Individual α -maps are combined across subjects, and a composite-basis approach—consisting of two successive PCA steps on the spatial dimension—is applied. Finally, Bayesian inference is performed on the reduced data, and the estimated covariate effects are projected back to voxel space.

We first parcellated the brain into regions of interest (ROIs) using the Automated Anatomical Labeling (AAL) atlas and applied the two-level dimensionality reduction strategy inspired by multi-scale factor analysis (MSFA) [Ting et al., 2018]. Within each ROI, we used singular value decomposition (SVD) to extract principal components explaining at least 99% of the variance in the projected long-memory values, capturing local spatial structure. We then applied a second-level SVD across the retained components to identify dominant modes of variation across the brain. The projection of the long-memory maps onto the composite basis space reduced the number of spatial locations from 29,639 voxels to 411.

The design matrix includes the following covariates: *Age* (continuous), *Medication Status* (binary indicator for whether ADHD-diagnosed subjects were taking medication), *ADHD Index* (a continuous score derived from the Conners' Parent Rating Scale—Long Version, or CPRS-LV, which reflects the severity of ADHD-related symptoms), and the interaction between *ADHD Index* and *Medication Status*. Thus, the design matrix has dimensions 355×5 . We estimated the regression coefficients using Bayesian inference with priors defined in Equation (6). The inverse-gamma hyperparameters were set to $(k, l) = (0.1, 0.5)$ to discourage high variances, as most variability was already captured through PCA. For the multivariate normal prior, we used $(\mu_0, \Lambda_0) = (0, 0.5 \times I)$. The full conditional distributions of $\beta_{PC_i}^*$ and $\delta_{PC_i}^2$ are available in closed form, allowing us to implement posterior sampling using a Gibbs sampler.

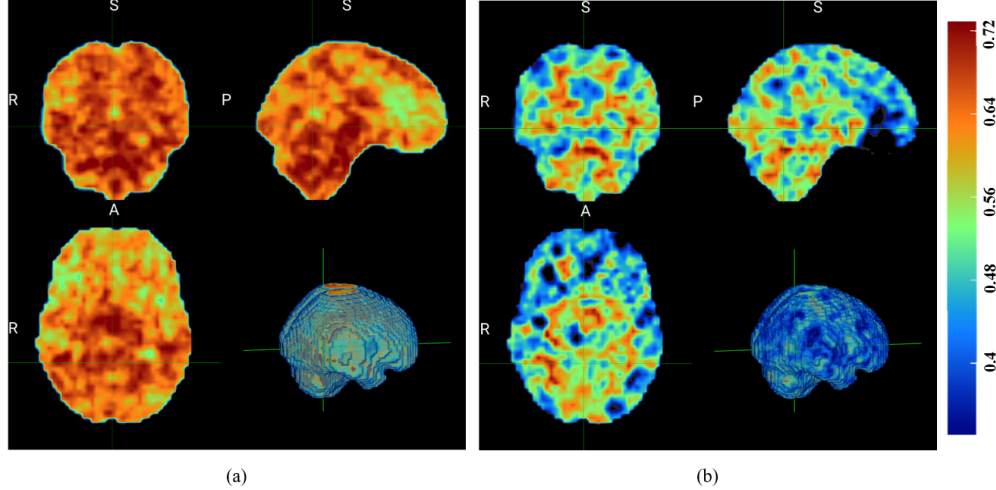


Figure 4: Average of long-memory maps of (a) 12-years-old or older subjects with no medication; (b) 9-year-old or younger subjects with medication.

The estimated regression coefficients β^* form a matrix of dimensions 5×411 , representing the effects of the five covariates on the 411 principal components. To recover voxelwise coefficient maps, we apply a two-step back-projection. First, the coefficients are projected from the global principal component space to the local ROI level. Then, they are multiplied by the corresponding eigenvectors within each ROI to reconstruct voxelwise estimates. This back-projection is performed at each MCMC iteration, yielding a sequence of voxelwise coefficient maps with dimensions $29,639 \times 5$. Because the reconstruction is based on a low-dimensional representation, the resulting maps are spatially regularized and exhibit reduced high-frequency noise.

To correct for multiple comparisons within the Bayesian framework, we construct joint credible bands over the entire brain volume using the approach of [Ruppert et al., 2003], as applied in similar neuroimaging contexts by [Meyer et al., 2015] and [Miranda and Morris, 2021]. This method controls the experimentwise error rate by accounting for the joint distribution of voxelwise estimates. At each MCMC iteration, we calculate the maximum standardized deviation across all voxels to determine a global threshold. Voxels whose $100(1 - \zeta)\%$ joint credible intervals exclude zero are flagged as active, ensuring that the probability of any false activation across the brain is bounded by ζ (the significance level).

To address the sparsity of significant voxels often encountered in whole-brain analyses, we applied a spatial clustering approach. Only spatially contiguous clusters comprising at least 50 voxels were retained for further analysis. This strategy enhances interpretability by focusing on spatially coherent regions of activation rather than isolated voxels. Figure 5 displays the coefficient map for the age variable, highlighting significant regions in the hippocampus and anterior lobe of the cerebellum that are associated with the long-range temporal dependence of the BOLD signal, as modeled by the long-memory parameter.

To assess the robustness of our findings to prior assumptions, we conducted a complementary frequentist analysis using voxelwise linear regression on the projected data. For each voxel, a t-test was performed, and results were corrected for multiple comparisons using the false discovery rate (FDR) at 0.05. Significant voxels were then clustered using the same spatial threshold as in the Bayesian analysis. Figure 6 presents a comparison between the Bayesian and frequentist results, including a map of their intersection. As shown, both methods identify overlapping regions of significance (highlighted by red circles in panel (c)). Notably, the Bayesian method yields more spatially extended regions of activation, reflecting its greater power to detect true effects by accounting for the spatial structure of the data—an advantage not present in the frequentist approach [Miranda and Morris, 2021].

4 Discussion

This study identified a positive association between age and the long-memory properties of resting-state fMRI signals in the hippocampus. The estimated linear regression coefficients indicate that increasing age is associated with higher values of the long-memory parameter, suggesting a developmental trend toward less persistent temporal structure in this region. Notably, no significant associations were observed between the long-memory parameter and the ADHD index, medication status, or their interaction.

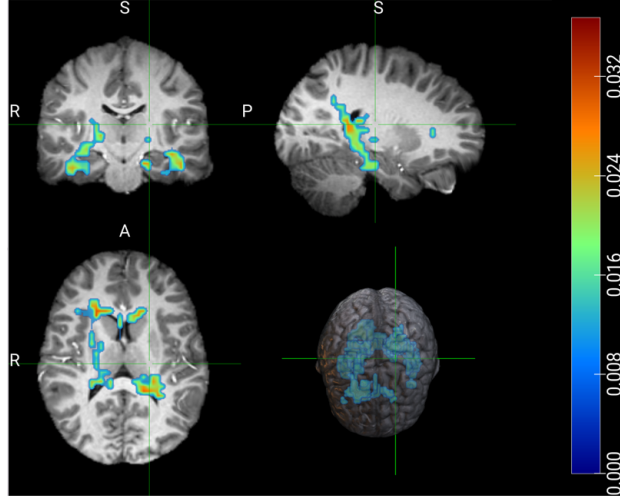


Figure 5: Coefficient map of the estimated β for age using Bayesian methods. The results are corrected for multiple comparisons at a significance level of 0.05, and only clusters larger than 50 voxels are retained.

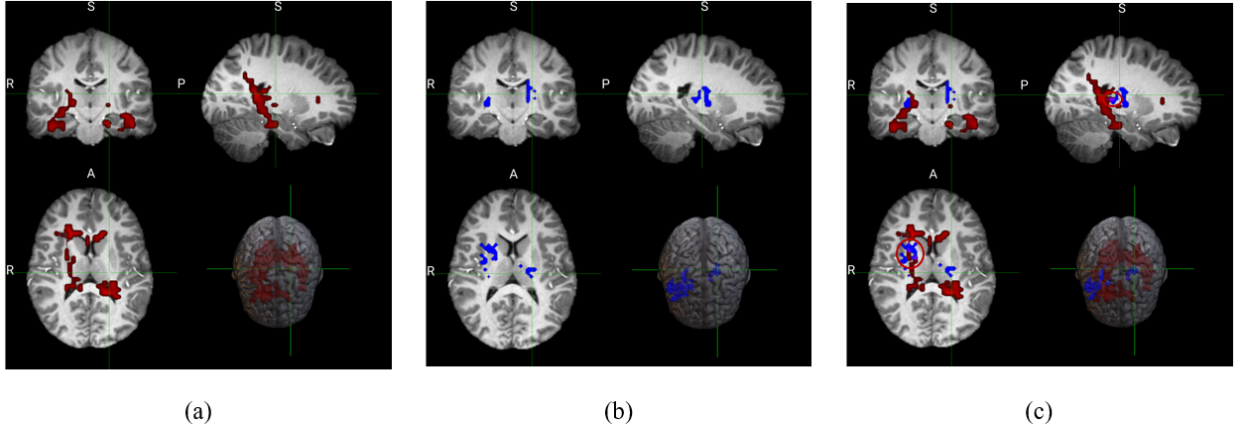


Figure 6: Binary maps of the estimated β coefficients for age using (a) Bayesian and (b) frequentist methods, each corrected for multiple comparisons using an FDR threshold of 0.05 and a cluster-size cutoff of 50 voxels. In (c), yellow regions indicate the intersection of significant voxels between both methods.

Prior studies have investigated the relationship between brain signal complexity and long-memory processes. For example, [Sokunbi et al., 2014] used the Hurst exponent to characterize reduced complexity in individuals with schizophrenia, while [Park et al., 2018] applied power spectral density (PSD) analysis to differentiate between patient groups, demonstrating its utility as a neuroimaging biomarker. More recently, [Medel et al., 2023] demonstrated a robust inverse relationship between the $1/f$ slope of the PSD—a proxy for long-memory—and Lempel–Ziv complexity (LZc), showing that time series with stronger long-range temporal structure (lower LM parameter) exhibited reduced complexity. This relationship was consistently observed across simulations, biophysical models, and empirical recordings. In light of these findings, we interpret the observed decrease in long-memory properties with age (higher α values) as reflecting a developmental shift toward less persistent but more complex brain signal dynamics.

The hippocampus, a medial temporal lobe structure, plays a central role in memory consolidation and spatial navigation. Structural imaging studies have shown that its volume undergoes substantial developmental changes, expanding rapidly in childhood and stabilizing by early adolescence [Reitz et al., 2009, Pfluger et al., 1999]. Longitudinal studies show that hippocampal volume continues to change during adolescence, with these changes linked to improvements in memory performance [Tamnes et al., 2014]. Beyond structural growth, functional changes also occur during development. In particular, greater signal complexity has been associated with healthier brain function, reflecting more flexible and efficient neural processing [Protzner et al., 2010]. Recent work highlights the role of inhibitory circuits in shaping

hippocampal plasticity, with evidence that both inhibitory gene expression and long-memory dynamics—indexed by the Hurst exponent—stabilize by late childhood [Nishio et al., 2024]. While hippocampal volume has long served as a marker of cognitive development, limitations of volumetric measures have prompted a shift toward cellular and functional metrics, such as dendritic complexity and neurogenesis [Roth et al., 2010]. In line with these findings, our study contributes to this literature by showing a positive association between age and the long-memory parameter, α , in the hippocampus, suggesting a developmental trajectory characterized by increasingly persistent—but potentially less complex—neural signals.

To the best of our knowledge, this is the first study to analyze voxel-wise temporal complexity of the brain in terms of long-memory properties. We developed a novel rs-fMRI analysis framework that integrates long-memory modeling with Bayesian inference and the discrete wavelet transform (DWT). The DWT offers a multiscale representation of the BOLD signal, which is particularly well-suited to capturing long-range temporal dependencies. This approach is followed by dimensionality reduction via a composite basis and group-level regression analysis to examine associations between spatial patterns of temporal complexity and subject-specific clinical covariates. By applying this framework, we identified associations between long-memory dynamics and age in the hippocampus that are relevant to brain development, offering new insights into the temporal organization of neural activity during childhood and adolescence.

Our approach addresses several key challenges in rs-fMRI analysis, including long-memory temporal dependence, high dimensionality, and the spatial structure inherent in the data. By leveraging a composite basis, we reduce dimensionality while capturing meaningful spatial and temporal patterns. These methodological advances contribute to a deeper understanding of the neural mechanisms involved in brain development and how they are reflected in the temporal dynamics of resting-state brain activity.

From a methodological standpoint, our analysis pipeline employs a two-stage approach. In the first stage, long-memory maps are estimated for each subject; in the second, these maps are related to subject-level covariates through group-level regression. While both stages rely on Bayesian inference via MCMC sampling, the uncertainty in the first-stage estimates is not formally propagated to the second stage. A fully Bayesian hierarchical framework that integrates subject-level inference with group-level analysis would provide a more complete characterization of the uncertainty with regards to inferences about associations with clinical covariates. Developing such a unified model is an important direction for future work.

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MCMC algorithm

First level analysis

To estimate the long-memory parameter (α) for each subject, we employed a Bayesian hierarchical model. The the joint posterior distribution for a single subject is given by:

$$p(\nu_v, \alpha_v | y) \propto (\det(\Sigma_v))^{-T/2} \exp\left(\frac{(y)^T (\Sigma_v)^{-1} y}{-2}\right) \times (\nu_v)^{-p-1} \exp\left(\frac{-s}{\nu_v}\right) \alpha_v^{a-1} (1 - \alpha_v)^{b-1} \quad (7)$$

Having the joint posterior density, the full conditional distribution for σ^2 is

$$p(\sigma^2|\alpha, y) \propto (\sigma^2)^{-\nu-N/2-1} \exp\left(\frac{-1}{\sigma^2} \left[\frac{y^T \Sigma^{-1} y}{-2} + \beta\right]\right) \quad (8)$$

$$\sigma^2|\alpha, y \sim \text{inv-gamma}(\nu' = \nu + N/2, \beta' = \frac{y^T \Sigma^{-1} y}{-2} + \beta) \quad (9)$$

and the full conditional distribution for α is

$$p(\alpha|\sigma^2, y) \propto (\det(\Sigma))^{-N/2} \exp\left(\frac{y^T \Sigma^{-1} y}{-2}\right) \alpha^{a-1} (1-\alpha)^{b-1} \quad (10)$$

where y is the transformed fMRI time series signal, Σ_v is the covariance function in the wavelet domain.

Figures 7 and 8 present examples of MCMC trace plots, density plots, and autocorrelation function (ACF) plots for the parameters, indicating good convergence.

Second level analysis

For the multi-subject analysis, we assumed a Gaussian likelihood for the observed data. The likelihood and prior distributions are specified as follows:

$$p(\alpha^*|Z, \beta^*, \delta^2) \propto (\delta^2)^{-N/2} \exp\left(\frac{(\alpha^* - Z\beta^*)^T (\alpha^* - Z\beta^*)}{-2\delta^2}\right) \quad (11)$$

$$p(\beta^*|\delta^2) \propto |\Lambda_0|^{-Q/2} \exp\left(\frac{(\beta_0 - \mu_0)^T \Lambda_0^{-1} (\beta_0 - \mu_0)}{-2}\right) \quad (12)$$

$$p(\delta^2) \propto (\delta^2)^{-k-1} \exp\left(\frac{-l}{\delta^2}\right) \quad (13)$$

The combination of these priors and the likelihood function forms the basis of our Bayesian inference, which leads to the full conditionals

$$\beta^*|\alpha^*, \delta^2 \propto MVN(\mu_n = (\Lambda_n)^{-1}(\mu_0^T \lambda_0 + Z^T \alpha^*), \Lambda_n = (Z^T Z + \Lambda_0^{-1})^{-1} \delta^2) \quad (14)$$

$$\delta^2|\beta^*, \alpha^* \sim \text{Inv-G}(k_n = k_0 + q/2, l_n = l_0 + 0.5((\alpha^*)^T \alpha^* + \mu_0 \Lambda_0 \mu_0 + \mu_n \Lambda_n \mu_n)) \quad (15)$$

where α^* is the vector of long-memory parameters estimated in first stage for all subjects, Z is the design matrix, β^* is the vector of regression coefficients, and δ^2 is the error variance.

Figure 9 displays example trace plots of the regression coefficients.

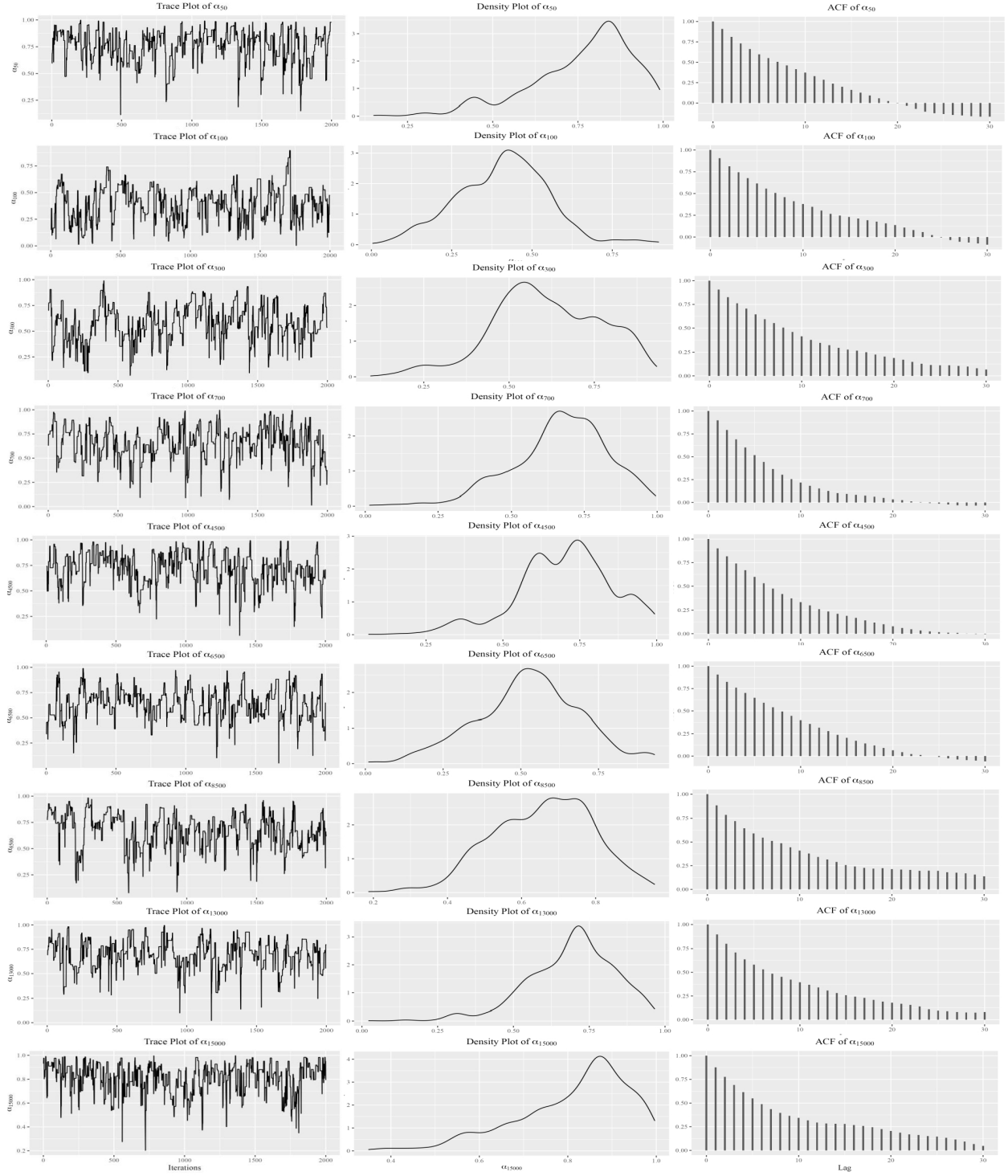


Figure 7: Diagnostic plots for the long-memory parameter, α , at randomly selected voxels. (a) Trace plot. (b) Density plot. (c) Autocorrelation function (ACF) plot.

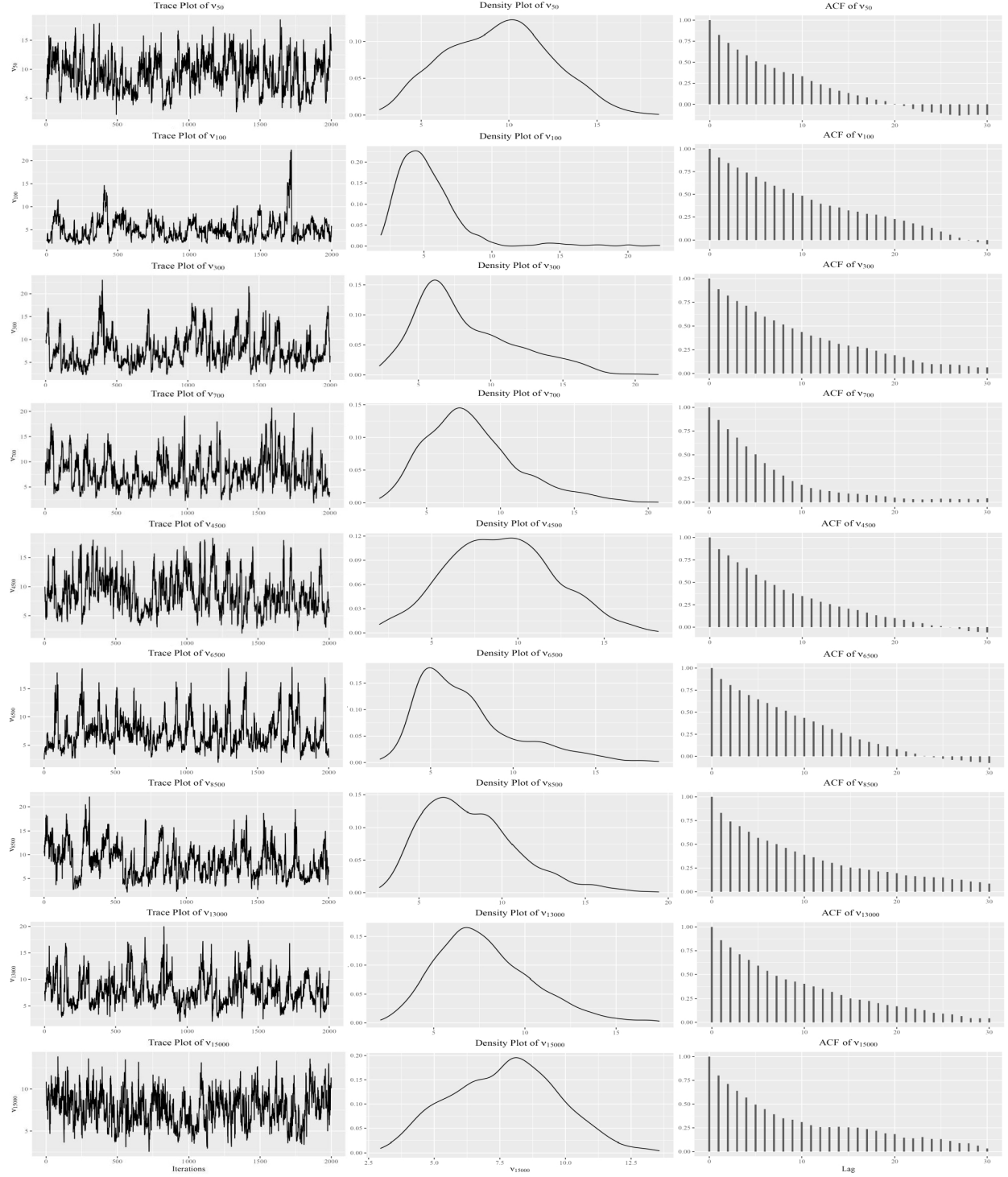


Figure 8: Diagnostic plots for the innovation variance, ν , parameter at randomly selected voxels. (a) Trace plot. (b) Density plot. (c) Autocorrelation function (ACF) plot.

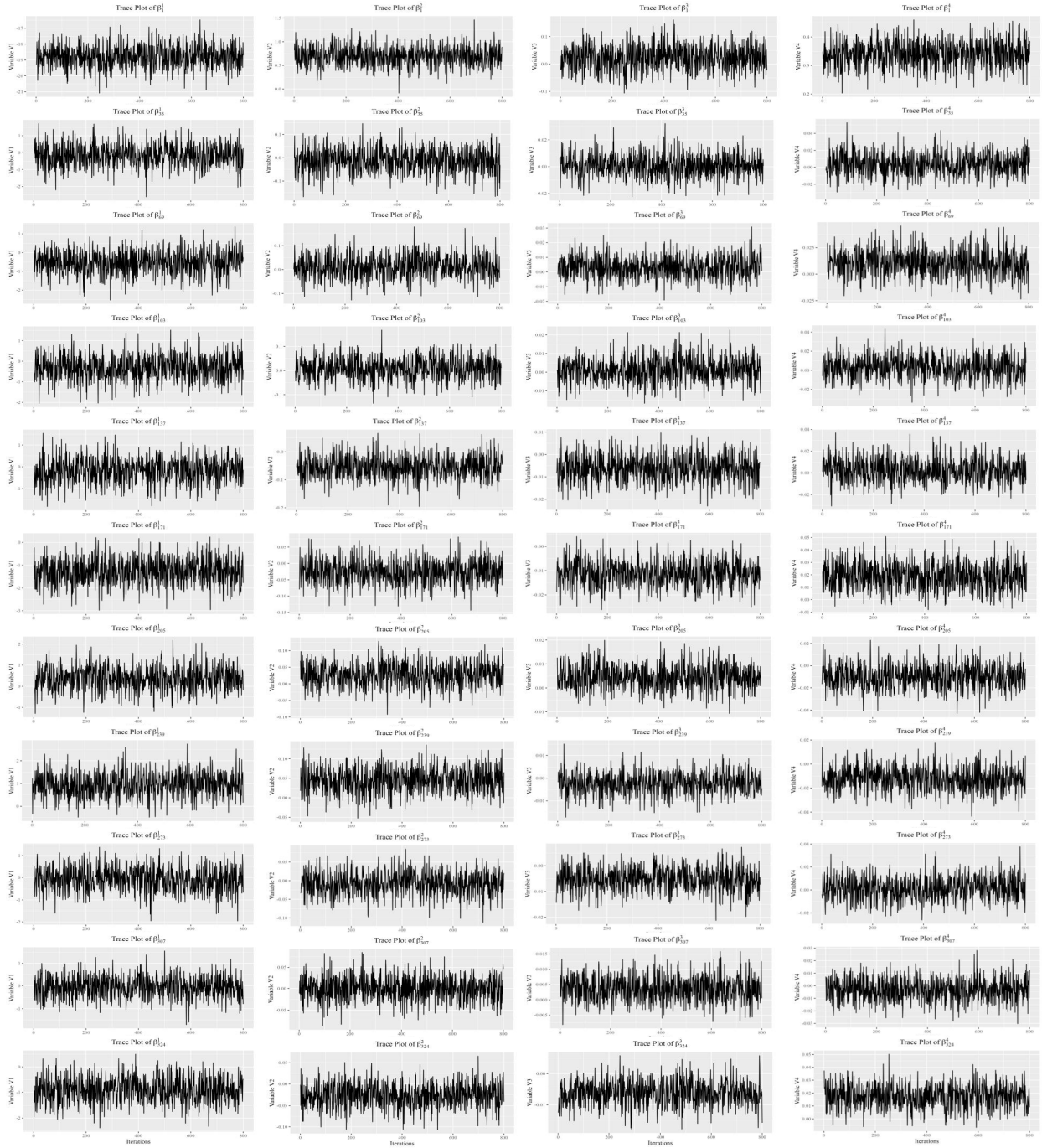


Figure 9: Trace plots of covariates projected onto principal component (PC) space. (a) Age. (b) Medication status. (c) ADHD index. (d) Interaction between ADHD index and medication status.