A parsimonious description of global functional brain organization in three spatiotemporal patterns

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Resting-state functional magnetic resonance imaging (fMRI) has yielded seemingly disparate insights into large-scale organization of the human brain. The brain’s large-scale organization can be divided into two broad categories: zero-lag representations of functional connectivity structure and time-lag representations of traveling wave or propagation structure. In this study, we sought to unify observed phenomena across these two categories in the form of three low-frequency spatiotemporal patterns composed of a mixture of standing and traveling wave dynamics. We showed that a range of empirical phenomena, including functional connectivity gradients, the task-positive/task-negative anti-correlation pattern, the global signal, time-lag propagation patterns, the quasiperiodic pattern and the functional connectome network structure, are manifestations of these three spatiotemporal patterns. These patterns account for much of the global spatial structure that underlies functional connectivity analyses and unifies phenomena in resting-state functional MRI previously thought distinct.
spatial structure. Zero-lag analyses capture the standing wave structure of these patterns, whereas time-lag analyses capture the traveling wave structure of these patterns. To capture these patterns in a single latent representation, we use a complex-valued extension of a popular dimension reduction technique: complex principal component analysis (CPCA).

In support of the second hypothesis, we begin with the observation that the resting-state functional MRI (fMRI) literature reveals very similar patterns of global BOLD activity across analytic approaches, including FC gradients, co-activation patterns (CAPs), independent component analysis (ICA) and other latent brain state methods as well as seed-based correlation analyses. We propose that these similar patterns across analysis methods are descriptions of the same underlying spatiotemporal patterns proposed in our first hypothesis. To test the second hypothesis, we compared a systematic survey of zero-lag and time-lag analyses to a set of spatiotemporal patterns derived from CPCA.

Our analyses revealed that three spatiotemporal patterns constitute the dominant large-scale spatial structure in spontaneous low-frequency BOLD fluctuations. With these three patterns, we can unify a range of previous findings in resting-state fMRI, including lag projections, the QPP, the topography of the global signal, the task-positive/task-negative pattern, the principal FC gradient and FC network structure. We demonstrate that all of these previous observations are manifestations of three spatiotemporal patterns captured within a unifying framework capable of modeling standing and traveling oscillatory BOLD phenomena. This novel framework allows for a parsimonious description of global functional brain organization that can inspire new hypotheses about the mechanisms underlying coordination of spontaneous activity across the brain.

Results
Standing and traveling wave simulation. We posit that the relative mixture of standing and traveling waves in cortical BOLD signals explains the spatial similarity between outputs of zero-lag and time-lag analyses. To test this claim, we first conducted a simulation study of varying degrees of traveling and standing spatiotemporal wave patterns.

Standing and traveling wave simulations (Supplementary Modeling Note 1) consisted of a back-and-forth sinusoidal oscillation of Gaussian curves on a two-dimensional grid (Fig. 1). This approach allowed us to systematically vary the degree of traveling wave behavior in each oscillation by adjusting the distance between Gaussian curve peak locations, from a distance of zero (‘pure standing’ motion) to a large distance (‘pure traveling’ motion). Zero-lag dimension-reduction techniques were applied to the time series of this simulated oscillation.

Zero-lag dimension-reduction analyses applied to pure standing waves effectively captured the oscillation in one latent factor (Fig. 1a; zero peak distance). Using Catell’s scree plot test, we identified the point at which the successive extraction of latent components exhibits a flattening in explained variance as the optimal number of components to extract. For pure standing motion, only the first eigenvalue was non-zero, confirming a single latent factor. Seed-based correlation analysis from a seed at the center of one Gaussian curve returned the same spatial pattern.

At non-zero distance between Gaussian curve peak locations, zero-lag analyses separated the non-synchronous motion into two components. The second eigenvalue of the correlation matrix increased with larger distance, indicating the presence of two latent components. The spatial patterns of these two components were largely consistent across methods. However, methods favoring spatial weight sparsity separated the traveling motion into isolated Gaussian curves, whereas non-sparse methods extracted separate phases or ‘snapshots’ of the overall oscillation.

Dimension-reduction techniques were extended into the complex-valued domain by augmenting the real-time courses of the grid into a complex signal via the Hilbert transform. To demonstrate the utility of complex-valued dimension-reduction methods in extracting traveling wave oscillations, we applied CPCA to the same empirical data simulations of traveling motion (Supplementary Modeling Note 1). Analogous to our diagnostics of the zero-lag correlation matrix, we constructed a scree plot consisting of the ordered eigenvalues from the complex-valued correlation matrix constructed from the complex grid time courses.

For pure traveling motion, the scree plot from the complex-valued correlation matrix revealed that only the first eigenvalue was non-zero, indicating the existence of a single latent factor (Fig. 1a; large peak distance). The grid amplitudes of the first complex principal component (PC) reflected the spatial distribution of the two Gaussian curves, indicating that the coherent fluctuations of the two Gaussian curves were captured by a single latent component. Notably, the phase-lag values of the first component precisely reflected the back-and-forth motion of the Gaussian curves.

In simulations with zero distance between peak locations, CPCA and zero-lag techniques converged on a similar solution. Furthermore, at smaller distances, the scree plots of the zero-lag and complex-valued correlation matrix both yielded a one-factor solution.

By construction, this simulation had access to the ‘ground truth’ mixture of traveling and standing wave components. No such ground truth is available in BOLD signals recorded from the brain. Thus, we invoked a ‘traveling index’ that measures the presence of traveling waves in CPCA components, varying from 0 (pure standing waves) to 1 (pure traveling waves). Such a metric provides a quantitative estimate of the mixture of traveling and standing waves in the absence of ground truth simulated data.

From the observation that zero-lag methods tend to split traveling Gaussian waves into separate latent components, we used the percentage of explained variance of the first eigenvector as a quality metric. The greater the explained variance, the more effectively zero-lag methods can capture traveling wave motion in a single latent component. We found a linear decrease in explained variance with traveling distance.

Fig. 1 | Simulation to analyze standing and traveling wave oscillations. a. Visualization of simulation and analysis results of traveling two-dimensional Gaussian curves at three peak distances (large, moderate and zero distance). For each simulation scenario, the bottom Gaussian curve moves upward (bottom to top) toward the top Gaussian curve. In the top-left panel of each simulation are four arbitrarily sampled timepoints. Note, the travel distance between the two Gaussian curves grows smaller at smaller peak distances (moving from the top to the bottom panel). The amplitude and phase-lag maps of the first complex PC from CPCA are shown in the bottom-left panel of each simulation. For all simulations, the amplitude and phase maps of the first complex component accurately describe the spatial distribution and phase-lag between the two Gaussian curves. In addition, the scree plot of the zero-lag (blue) and complex-valued (green) correlation matrix is displayed. Results of various zero-lag FC analyses are displayed in the right panel. For the dimension-reduction techniques, two components were estimated at non-zero peak distances, motivated by the non-zero second eigenvalue of the correlation matrix. For zero-peak distance, only a single component was estimated. At non-zero peak distances, zero-lag dimension-reduction techniques tend to split the traveling wave oscillation into either (1) separate Gaussian curves (varimax) or (2) separate phases of the oscillation. b. From left to right, plots of the traveling index by peak distance, the variance explained by the first eigenvalue (zero-lag correlation matrix) by peak distance and the variance explained by the first eigenvalue by traveling index.
variance moving from values beyond 0.2 to larger values of the traveling index (Fig. 1b). Overall, we found that, for moderate values of the traveling index (<0.5), the explained variance of the first eigenvector is greater than 80%. This suggests that zero-lag methods effectively capture a large majority of the variance of a spatiotemporal pattern with moderate traveling wave behavior. For systems
**Fig. 2 | Form and properties of three prominent spatiotemporal patterns.** Phase delay maps and reconstructed timepoints of the first three complex PCs. Phase delay maps represent the temporal ordering (in seconds) of cortical vertex BOLD time series within the spatiotemporal pattern. Phase delay maps describe a repeating or cyclical pattern expressed in radians (0 to 2π) around a unit circle, where a phase value of 0 corresponds to the beginning of the spatiotemporal pattern, and 2π corresponds to the end of the spatiotemporal pattern. For clarity, radians are converted to temporal units (seconds) (Methods). The values in the phase delay map correspond to the temporal delay (in seconds) between two cortical vertices, such that smaller values occur before larger values. Values are mapped to a cyclical color map to emphasize the cyclical temporal progression of each spatiotemporal pattern. To illustrate the temporal progression of the spatiotemporal patterns, six reconstructed timepoints are displayed for each pattern. The phase delay map and reconstructed timepoints are shown for the first spatiotemporal pattern (a)—‘pattern one’; the second spatiotemporal pattern (b)—‘pattern two’; and the third spatiotemporal pattern (c)—‘pattern three’.
consisting predominantly of standing waves or a moderate degree of traveling waves, we expect solutions of time-lag and zero-lag FC methods to converge.

**Three prominent spatiotemporal patterns.** To understand the standing and traveling wave components that underlie empirical spontaneous BOLD fluctuations, we applied CPCA to a random

**Fig. 3** | **Form and properties of three prominent FC topographies.** **a**, The spatial absolute-valued correlation between the first three PC maps and each FC topography displayed as a table. All correlations are rounded to the second decimal place. The color of each cell in the table is shaded from light yellow (strong correlation) to dark blue (weak correlation). All FC topographies in our survey exhibited strong spatial correlations (Pearson’s correlation) with one (or two) of the first three PCs. **b**, The first three PC spatial maps. **c**, The scree plot that displays the explained variance in cortical time series for each successive PC. The scree plot indicates a clear elbow after the third PC, indicating a ‘diminishing return’ in explained variance of extracting more components. Clus, cluster; Comp, component; P, precuneus; SMG, supramarginal gyrus.
sample (n = 50) of resting-state fMRI scans (Human Connectome Project (HCP) Young Adult S1200 release). We downsampled the surface-based cortical time series to approximately 5,000 vertices. All analyses were successfully replicated in an independent sample (n = 50) of unrelated HCP participants (Supplementary Figs. 1 and 2).

To choose the number of CPCA components to extract, we used the Catell’s scree plot test applied in our simulations (Fig. 1a). This criterion indicated a clear flattening in explained variance beyond three PCs (Supplementary Fig. 3). The three leading complex PCs represent the top three dimensions of variability across complex-valued cortical BOLD time series. Associated with each complex PC is a phase delay map, reflecting the time delay (in seconds) between cortical vertices (Methods). To examine the temporal progression of each complex PC, we sampled the reconstructed BOLD time series from each component at multiple, equally spaced phases of its cycle (n_phase = 30; Methods). Movies of the reconstructed BOLD time courses are displayed in Supplementary Movie 1. Detailed descriptions of the spatiotemporal patterns of each complex PC, and comparisons of their propagation patterns, are provided in Supplementary Fig. 4. Complex PC phase delay maps beyond the first three are in Supplementary Fig. 5.

The first component (‘pattern one’), representing the leading axis of variance, explains 21.4% of the variance in intrinsic BOLD time series, more than three times the variance explained by the second (6.8%) or third (5.7%) component. The traveling index of the first component was 0.25, indicating a largely standing spatiotemporal pattern, with some traveling wave behavior. The dynamics can be separated into two phases. In the first phase, negative cortex-wide BOLD amplitudes are observed that are strongest in the sensorimotor (SM) cortex, superior parietal (SP) lobule, lateral visual (LV) cortex and superior temporal (ST) gyrus (Fig. 2a and Movie 1). We refer to these brain regions as the somato-motor-visual (SMLV) complex, noting that it also includes some regions outside sensorimotor cortices (for example, SP and ST). The second phase exhibited a propagation of strong negative BOLD amplitudes in the SMLV toward cortical regions overlapping primarily with the frontoparietal network (FPN) but also with the DMN and V1. This entire spatiotemporal sequence of negative BOLD amplitudes was followed by a spatiotemporal sequence with positive BOLD amplitudes with the same dynamics.

The second component (‘pattern two’) was the most stationary of the first three components, with a traveling index of 0.14. The overall spatiotemporal pattern can be described as an anti-correlated oscillation between SMLV regions and the DMN. Interestingly, this pattern of anti-correlation or bipolar contrast appeared to delineate the unipolar (all-negative) contrast in the first phase of the first complex PC. Visual inspection revealed a minor traveling wave pattern propagating out from the SM region to the premotor cortex (anterior direction) and SP (posterior direction) in between peak amplitudes of the anti-correlated oscillation.

The third component (‘pattern three’) was similar to the first component with a traveling index of 0.27. The dynamics can be split into two phases. In the first phase, strong negative amplitudes are observed in the SM, ST and LV, with weak negative amplitudes in the DMN; strong positive amplitudes are observed in the inferior parietal (IP) lobule, inferior temporal (IT) gyrus, premotor cortex, dorsolateral prefrontal cortex (DLPFC) and V1. The second phase was marked by propagation from the IP lobule (anterior direction) and premotor (posterior direction) toward the SM cortex and the IT gyrus (posterior direction) toward the LV cortex.

To further understand what properties of the cortical BOLD time courses give rise to the time-lag structure of the three spatiotemporal patterns, we conducted two null model exercises. First, BOLD time courses were randomly shuffled to demonstrate that the time-lag structure of the spatiotemporal patterns depends on properties of the time courses beyond their zero-lag correlations. Random shuffling of the time courses preserves the zero-lag correlation structure while eliminating time-lag correlation structure. As expected, CPCA of time-point shuffled data removes the intermediate phase delays (between 0 and π), leaving behind a pure standing wave structure (Supplementary Fig. 6).

Second, we simulated time courses from a first-order multivariate autoregression (VAR(1)) model fit to the cortical BOLD time series. This model leaves the time-lag (that is, autoregressive) structure of the cortical BOLD time courses intact while assuming Gaussianity, linearity and stationarity of the time courses26. CPCA of the simulated time courses generated from the VAR(1) model replicated both the zero-lag and time-lag structure of the three spatiotemporal patterns (Supplementary Fig. 6). These findings suggest that the three spatiotemporal patterns arise from properties of the BOLD time courses that are mostly Gaussian, linear and stationary.

FC topographies reflect the three spatiotemporal patterns. The three spatiotemporal patterns are predominantly composed of standing waves. This finding, and the results of the simulation study (Fig. 2), suggests that zero-lag FC methods should capture most of the variance in these spatiotemporal patterns. We selected a large number of commonly used zero-lag FC methods and applied them to the original time courses from the same resting-state fMRI data. Dimension-reduction methods included principal component analysis (PCA), PCA with Varimax rotation (varimax)24, Laplacian eigenmaps (LEs)25, spatial independent component analysis (SICA)25 and temporal independent component analysis (TICA)25. Hidden Markov models (HMMs), which are commonly

Fig. 4 | Similar propagation patterns between average latency structure and pattern one. Comparison between the average latency structure of spontaneous BOLD fluctuations and the phase delay map of pattern one. The lag projection map (left) represents the average time delay (in seconds) between each vertex of the cortex. The circular average map (middle) represents the average phase delay (in radians) between each vertex of the cortex. As in Fig. 2, the pattern one phase delay map (right) represents the phase delay (in radians) between the vertices within the dynamics of pattern one. The two methods for computing average latency structure exhibiting strong agreement in their propagation patterns (r = 0.83). The strong similarity between the average latency structure and pattern one phase delay map (r = 0.98) indicates that the average latency structure is primarily driven by the spatiotemporal dynamics of pattern one.
used latent state space models for estimating brain states\textsuperscript{17}, were also included. Seed-based FC analysis methods included seed-based correlation analysis\textsuperscript{6} and CAP analysis\textsuperscript{15} with k-means clustering of suprathreshold timepoints into two clusters. Seed-based methods were run for three key seed locations corresponding to major hubs—in the SMLV, DMN and FPN—the somatosensory cortex, precuneus and dorsolateral prefrontal cortex\textsuperscript{4}. Results were identical for alternatively placed seed regions within these three networks (Supplementary Fig. 7).

To determine a meaningful number of dimensions in our latent dimension-reduction analyses (PCA, varimax PCA, LE, SICA, TICA and HMM), we again used the scree plot criterion. The scree plot of the zero-lag correlation matrix indicated a clear flattening in explained variance after three PCs (Fig. 2c).

To compare FC topography spatial similarity, we used the spatial correlation between the cortical vertex weight values of each topography. To summarize FC topography similarities, we compared each topography to the first three PC maps computed from PCA. Similarly to the first complex PC of CPCA, the first PC explains 20.4% of the variance in BOLD time series, more than three times the variance explained by the second (6.8%) or third (6.1%) PC. Each FC topography exhibits strong similarities with one or more of the first three PCs (\(r > 0.6\)) (Fig. 3a). Statistical significance of the spatial correlation between each FC topography and its most strongly correlated PC was computed using spin permutation tests\textsuperscript{27} (\(n_{\text{samples}} = 1,000\)). All correlation pairs were statistically significant (\(P = 0.001\), lower limit of permutation test). However, there was notable variability in the strength of correlations between each FC topography and one or more of the PCs. Furthermore, strong similarities between FC topographies are seen for more than one PC. Detailed results of seed-based regression/CAP and dimension-reduction analyses are provided in Supplementary Figs. 8 and 9. Overall, our survey revealed a considerable consistency in FC topographies across methods.

Comparison of the spatial weights of the three PCs (Fig. 3b) with the spatiotemporal patterns (patterns one, two and three) of the three complex PCs (Fig. 2) illustrates that both methods capture similar spatiotemporal patterns. The correspondence was one to one—the first PC matching pattern one, the second PC matching pattern two and the third PC matching pattern three. The static spatial weights of each PC appeared as a ‘snapshot’ within their corresponding spatiotemporal pattern: PC1-pattern one (\(r = 0.998, t = 11.9\) seconds), PC2-pattern two (\(r = 0.986, t = 12.6\) seconds) and PC3-pattern three (\(r = 0.972, t = 3.7\) seconds). Furthermore, the three spatiotemporal pattern time courses closely tracked the first three PC time courses: PC1-pattern one (\(r = 0.998, t = 11.9\) seconds), PC2-pattern two (\(r = 0.986, t = 12.6\) seconds) and PC3-pattern three (\(r = 0.972, t = 3.7\) seconds). The static spatial weights of each PC appeared as a ‘snapshot’ within their corresponding spatiotemporal pattern: PC1-pattern one (\(r = 0.998, t = 11.9\) seconds), PC2-pattern two (\(r = 0.986, t = 12.6\) seconds) and PC3-pattern three (\(r = 0.972, t = 3.7\) seconds). Given the similarity, we refer to the patterns produced by standard PCA and CPCA as patterns one, two and three, interchangeably.

Comparison with previously observed resting-state phenomena. A further aim of this study was to understand the relationship between these three spatiotemporal patterns and previously observed phenomena in intrinsic BOLD signals. Lag projections\textsuperscript{7} and the QPP\textsuperscript{18} correspond to time-lagged phenomena at shorter (\(\approx 2\) seconds) and longer (\(\approx 20\) seconds) time scales, respectively. Lag projections are computed from the average pair-wise time delays between BOLD time courses and represent the average ‘ordering’ in time of BOLD amplitude peaks across the brain. An analogous time delay representation can be computed from the average of the

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**Fig. 5 | The task-positive/task-negative pattern, primary FC gradient and pattern two describe the same spatiotemporal pattern.** a. From left to right: pattern two, task-positive/task-negative (TP/TN) pattern and the PG represented by the spatial weights of the second PC from PCA (sign flipped for consistency), seed-based correlation map (precuneus seed) and first LE with no thresholding of the affinity matrix, respectively. Similar spatial patterns are produced from all three analyses—pattern two: TP/TN (\(r = 0.96\)) and pattern two: PG (\(r = 0.83\)). b. The effect of FC matrix percentile thresholding on the resulting spatial weights of the PG, computed as the first eigenmap of the LE algorithm (left hemisphere). At zero to low thresholding of the FC matrix, the first LE resembles pattern two (PC2). As the threshold is raised, the spatial weights of vertices within the DMN and SMLV become more uniform. At higher thresholds, this results in an eigenmap that resembles pattern one.
QPP pattern exhibits a global pattern of activity with positive correlation across brain regions (‘global’ QPP), and the other QPPs exhibit the same direction of propagation (Fig. 4). Interestingly, both anti-correlated QPPs and the temporal dynamics of pattern two and the anti-correlated QPP exhibited a strong spatial similarity with the global QPP overlapped significantly (Supplementary Movie 2). This suggests that the task-positive versus task-negative pattern arises from the anti-correlated dynamics between the SMLV and DMN represented by pattern two.

We hypothesized that the global QPP and anti-correlated QPP correspond to the dynamics of pattern one. We constructed a dynamic visualization of the global signal through a peak-averaging procedure. Specifically, all BOLD time courses within a fixed window (15 TRs on each side) were averaged around randomly sampled peaks (n = 200, >1 standard deviation above the mean) of the global mean time course. This revealed that the temporal dynamics surrounding peaks of the global signal precisely match those of pattern one (Supplementary Movie 2).

The temporal dynamics of pattern two largely represent an anti-correlated pattern between the SMLV and the DMN. This resembles the task-positive/task-negative anti-correlation pattern originally observed by Fox et al. and Fransson. We reproduced these results by creating whole-brain vertex-wise correlation maps using a seed time course from the left and right precuneus, a key DMN node. As expected, an anti-correlated pattern was observed between the SMLV and DMN (Fig. 5a). Additionally, the precuneus seed whole-brain correlation spatial map precisely corresponds to the pattern of BOLD activity at peak amplitudes of pattern two (CPC1: r = 0.92, t = 1.8 seconds). This suggests that the task-positive versus task-negative pattern arises from the anti-correlated dynamics between the SMLV and DMN represented by pattern two.

A similar anti-correlation pattern to the task-positive/task-negative pattern has been observed in the FC gradient literature and is known as the principal FC gradient (PG). In our zero-lag FC survey (Fig. 3), we computed the PG as the first component derived from LE precisely resembles the BOLD activity at peak amplitudes of pattern two (PC1: r = 0.71; Fig. 5a). The PG resembles the anti-correlated spatial structure of pattern two, but this similarity depends on the level of thresholding of the FC matrix input to the LE algorithm (Fig. 5b). The FC matrix represents Pearson’s correlation of BOLD time courses between all pairs of cortical vertices (that is, correlation matrix). Generally, thresholding is performed row-wise or column-wise on the FC matrix (for example, 90th percentile of correlation values within that row). If no FC matrix thresholding is performed, the first eigenvector produced from LE precisely resembles the BOLD activity in pattern two (PC2: r = 0.83; Fig. 5a). As the percentile threshold applied to the FC matrix increases, the spatial weights of vertices within the DMN and SMLV become more uniform (Fig. 4b). At higher percentile thresholds (for example, 90th percentile), a contrast between the SMLV and DMN appears that is similar to the bipolar contrast of pattern one (PC1: r = 0.83) and the anti-correlation contrast of pattern two (PC2: r = 0.82). The reason that the first component of LE returns pattern two, over the more prominent pattern one, is due to timepoint centering (Supplementary Fig. 11).
Network-based representations of FC. The network or graph-based approach to FC analysis models the structure of pair-wise relationships between BOLD time courses. We investigated the degree to which the structure of pair-wise relationships between BOLD time courses arises from the dynamics of the three spatiotemporal patterns. An FC matrix was constructed by computing correlations between all pairs of cortical BOLD time courses (Fig. 6). We compared this matrix to the reconstructed FC matrix from the three spatiotemporal patterns. We estimated the similarity between the two FC matrices by computing the correlation coefficient between the lower triangles of each matrix. Despite a larger mean correlation in the reconstructed FC matrix, we found that the FC matrices were strongly correlated ($r = 0.77$).

We also sought to determine whether the community structure of cortical BOLD time courses can arise from the shared dynamics of the three spatiotemporal patterns. We estimated network communities from the original and reconstructed FC matrix using the Louvain modularity maximization algorithm. A measure of similarity between community structures, normalized mutual information (NMI), showed strong community structure similarity between the original and reconstructed FC matrix (NMI = 0.73).

Discussion

The goal of this study was to provide a parsimonious taxonomy of prominent global spatiotemporal patterns in spontaneous BOLD activity to enable insight into the functional architecture of the human brain. Using a complex-valued extension of PCA, we identified three prominent spatiotemporal patterns consisting primarily of standing waves with some traveling wave behavior. Consistent with our simulations, the relative predominance of standing over traveling wave structure ensured that zero-lag FC methods effectively captured much of their spatiotemporal structure. This finding explains previous observations that traveling waves of BOLD activity resemble patterns of large-scale FC topographies.

A notable finding from this study was the ubiquitous presence of three spatiotemporal patterns across a wide variety of zero-lag FC techniques. Several zero-lag FC methods (ICA, varimax and HMM) involved an initial PCA dimension-reduction step. Thus, the common patterns resulting from zero-lag FC methods may be caused by a common reliance on PCA. However, an ample number of studies demonstrate that the output similarity across these methods is not guaranteed but depends on the area of application. Furthermore, the same patterns emerged from zero-lag FC methods that do not rely on PCA (for example, CAP and seed-based correlation) and also from time-lag analyses with no relation to PCA (QPP and lag projection).

Another core finding of our study is the identification of the brain's average latency structure (Fig. 4) with pattern one. This latency structure, originally discovered by averaging the pair-wise time delays between brain regions, was found to map directly to the phase delay pattern of pattern one. In other words, the average latency structure of spontaneous BOLD fluctuations reflects the traveling wave structure of the dominant spatiotemporal pattern (pattern one). Furthermore, a repeated peak-averaging procedure demonstrated that this time-lag structure corresponds to local propagation patterns surrounding peaks of the global mean time course. This is consistent with previous findings of a global propagating wave event surrounding peaks of the global mean time course.

Although time-varying or dynamic FC was not examined in this study, fluctuations between the spatiotemporal patterns identified here may explain the variability in zero-lag FC structure over time. For example, a new time-varying FC analysis, known as edge time series analysis, has found that patterns of co-fluctuations in zero-lag FC resemble the spatial structure of the three spatiotemporal patterns. Although non-stationarity of zero-lag FC is a controversial topic, modeling work has shown that time-varying FC is consistent with stationary time series models. Our null modeling results (Supplementary Fig. 6) suggest that a stationary, linear autoregressive process sufficiently describes the zero-lag and time-lag correlation structure of the three spatiotemporal patterns.

As the primary aim of our study was descriptive, we have avoided any explanatory or causal explanation of the possible neuronal or non-neuronal origins of these three spatiotemporal patterns. However, the identification of pattern one with the global mean time course suggests potential candidate causal mechanisms. One promising candidate is a systemic circulatory origin. A considerable portion of low-frequency BOLD signal variance is correlated with systemic oxygenation fluctuations in the periphery. This low-frequency peripheral oscillation tracks the global mean fMRI time course and exhibits traveling wave behavior induced by differential blood transit time in the cerebral vasculature. Potential sources of this systemic circulatory effect include vasomotion, fluctuations in arterial CO$_2$ and/or Mayer waves. However, other studies support a neural origin for the global signal. Momentary fluctuations in arousal and/or vigilance are also related to the global BOLD signal. Some physiological processes strongly co-occur with cortical excitability, making it even more difficult to disentangle the neural versus non-neural sources of the BOLD fluctuations.

Taken together, these findings suggest that the global signal (and, by extension, pattern one), although influenced by vascular and other systemic physiological sources, is at least partially driven by neuronal sources. The current study does not resolve these questions about the sources of the BOLD fluctuations and underscores the importance of understanding vascular components of the global signal to effectively denoise fMRI data while preserving neuronal signals.

Candidate origins of patterns two and three are more difficult to identify. Pattern two closely resembles the task-negative/task-positive pattern originally discovered in resting-state fMRI. A similar anti-correlated pattern is consistently observed in response to task stimuli. Pattern two strongly resembles the QPP obtained after global signal regression, which has been linked to infraslow electrical activity. Patterns of propagating activity have also been observed in optical fluorescence imaging and electrophysiological recordings, which demonstrates that time-lagged relationships can arise from neural as well as hemodynamic processes. Future research may be directed toward a more complete understanding of the common or distinct neuronal or physiological mechanisms that give rise to these spatiotemporal patterns.

Although these three spatiotemporal patterns explain a large portion of variance in spontaneous BOLD fluctuations (~32%), a considerable portion of variance is left unexplained. Notably, these three components did account for much of the observed whole-brain functional connectivity. Thus, the remaining, larger fraction of variance may contribute less to the global spatial structure of BOLD signals. The sources of this remaining signal component remain unclear. Although some portion is likely to arise from non-neural effects, there is an intriguing possibility that it also contains activity related to ongoing cognition. We speculate that it may reflect more spatially focal variance in spontaneous BOLD fluctuations, possibly more closely related to neurovascular coupling than the global patterns observed in this study.

It is important to qualify the assumptions on which our comparisons were based. First, the primary metric that determined the number of latent dimensions in our analysis was explained variance. The number three was chosen based on the observation of diminishing
explained variance with increasingly higher-dimensional solutions. Although alternative methods for the choice of dimensionality have been proposed, we found that the criterion of explained variance achieved high robustness. Second, most of the analysis approaches that we surveyed can reveal finer-grained spatial insights at higher component or cluster numbers (for example, ICA or variimax PCA). However, we do not expect the same consistency in analytic approaches at finer-grained levels of analysis. Empirical examination of consistency in zero-lag FC analyses at solutions greater than three components confirms this: higher-dimensional solutions yield less consistent FC topographies (Supplementary Fig. 12). Notably, the consistency of analysis approaches at our low-dimensional level of analysis suggests that these three spatiotemporal patterns are robust phenomena. Finally, these three spatiotemporal patterns were modeled at the population level; inter-participant variability in the spatial structure of these patterns was not considered in our analyses. However, an examination of the first three PCs across a sample of participants reveals notable inter-participant variability in their spatial structure (Supplementary Fig. 13).

In summary, we identified three spatiotemporal patterns that parsimoniously recapitulate major findings from a wide range of analytical techniques. Furthermore, these patterns account for much of the large-scale structure that underlies all FC analysis and, therefore, affect how everything from functional networks to graphs are interpreted. As the study of the brain as a complex system advances, these three spatiotemporal patterns have potential applications in better constraining generative models of brain activity, predicting variability in response to external stimuli, informing targeted modulation of brain activity to achieve a particular state and understanding interactions between global brain states and localized activity in neuronal circuits. The concise characterization of systems-level brain activity in three spatiotemporal patterns will facilitate the cross-scale research needed to link fundamental neuroscience studies and human behavior.

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Methods

Resting-state fMRI data. Our study used resting-state fMRI scans from the HCP S1200 release\(^{17}\). Participants were unrelated, healthy young adults (ages 22–37 years). Resting-state fMRI data were collected over two consecutive days for each participant and two sessions, each consisting of two 15-minute runs, amounting to four resting-state scans per participant. Within a session, the two runs were acquired with opposite phase-encoding directions: L/R encoding and R/L encoding. We selected a single 15-minute scan from a random sample of participants (n = 50, 21 males) on the first day of scanning. We balanced the number of L/R and R/L phase-encoding scans across our participants (n = 25 for each encoding direction) to ensure that results were not biased by acquisition from any given phase-encoding direction. We chose a single 15-minute scan per participant to ensure that the phase-encoding/phase-decoding parameter and the imaging session (two resting-state scans per imaging session) did not differ within the same participant. A second independent random sample of participants (n = 50, 29 males) was selected as a validation sample. We selected surface-based CIFTI resting-state fMRI scans (MSMall registered) that had been previously pre-processed with the HCP’s ICA-based artifact removal process\(^{48}\) to minimize effects of spatially structured noise in our analysis. All brain imaging data were acquired on a customized Siemens 3T Skyra at Washington University in St. Louis using a multi-band sequence. The structural images were 0.7-mm isotropic. The resting-state fMRI data were at 2-mm isotropic spatial resolution and with TR = 0.72 seconds. Further details of the data collection and pre-processing pipelines of the HCP can be found elsewhere\(^{49-50}\). Informed consent was obtained from all participants, and all methods were carried out in accordance with relevant guidelines.

Resting-state fMRI pre-processing. Resting-state fMRI scans were spatially smoothed with a 5-mm full width at half maximum kernel using the surface-based smoothing algorithm in Connectome Workbench version 1.4.2. Resting-state fMRI signals from each vertex were then temporally filtered to the conventional low-frequency range of resting-state fMRI studies using a Butterworth band-pass zero-phase filter (0.01–0.1 Hz). Due to (1) the computational complexity of our analytic pipeline, owing to the large number of analyses studied, and (2) our interest in global, spatially distributed patterns, resting-state fMRI scans were then resampled to the fsaverage space from FreeSurfer\(^{51}\). This step downsampled the total number of vertices in the left and right cortex to 4,800 vertices. In group analyses, we Z-scored (to zero mean and unit variance) the BOLD time series from all vertices before temporal concatenation of individual scans. All analyses were applied to group-level data formed by temporal concatenation of participant resting-state scans.

CPCA. To extract traveling wave patterns, we applied PCA to complex BOLD signals obtained by the Hilbert transform of the original BOLD signals. We refer to this analysis as CPCA. This technique has been referred to as complex Hilbert empirical orthogonal functions in the atmospheric and climate sciences literature\(^{52}\) or complex orthogonal decomposition in the engineering and physics literature\(^{53}\). CPCA allows the representation of time-lag relationships between BOLD signals through the introduction of complex correlations between the Hilbert-transformed BOLD signals. The original time courses and their Hilbert transforms are complex vectors with real and imaginary components, corresponding to the non-zero-lagged time course (t = 0) and the time course phase shifted by t = pi/2 radians, respectively. The correlation between two complex signals is itself a complex number (composed of a real and imaginary part) and allows one to derive the phase offset (and magnitude) between the original time courses— that is, the time-lag at which the correlation is maximum. CPCA applied to the complex-valued correlation matrix produces complex spatial weights for each PC that can give information regarding the time-lags between BOLD time courses. In the same manner, the complex signal can be represented in terms of amplitude and phase components (via Euler’s transform), the real and imaginary components of the complex PC can be represented in terms of amplitude and phase spatial weights. Of interest in this study is the phase delay spatial map that represents the time-lag between pairs of BOLD time courses—that is, those cortical vertices with a low phase value activate earlier than cortical vertices with a high phase value. Notably, the PCs from the CPCA retain the same interpretive relevance as the original PCA—the first n PCs represent the top n dimensions of variance in the Hilbert-transformed BOLD signals. CPCA was implemented with singular value decomposition of the group-wise temporally concatenated complex-valued time series using the fast randomized singular value decomposition (SVD) algorithm developed by Facebook [https://github.com/facebookarchive/hpca].

Estimating the time scale of complex PCs. For simplicity, the phase spatial maps of each complex PC are displayed in seconds (Fig. 2) as opposed to radians. However, the conversion of phase values (in radians) to time units (seconds) required for an estimation of the time scale of each complex PC is straightforward. Maps of the complex PCs have no characteristic time scale other than that imposed by our band-pass filtering operation (0.01–0.1 Hz—that is, 100 seconds in 10 seconds) in the pre-processing stage. To approximate a unique time scale within this frequency range for each component, we calculated the average duration for a full oscillation of each complex PC using the temporal phase of the complex component time series. This was calculated by fitting a linear curve to the unwrapped temporal phases of the complex PC time series. The slope of the line was then used as an estimate of the average duration of a TR (0.72 seconds) or timepoints. To estimate the average duration in TRs of a full oscillation, we divided a full oscillation (2 radians) by the duration in radians of a TR. For example, for a TR duration of 0.5 radians, the duration of a full oscillation (2 pi radians) would be approximately 12.6 TRs. Using this procedure, we found that the average duration of the first three complex PCs was 28 seconds (38.7 TRs), ~27 seconds (37.4 TRs) and ~28 seconds (39.1 TRs), respectively. Using this duration as an estimate of the characteristic time scale of each complex PC allows us to provide an estimate of the time delay in seconds of the spatial phase map. For example, for the first complex PC, a 360° (2 pi radians) phase difference between two cortical BOLD time series would correspond to a ~28-second time-lag between the time series. A smaller phase difference between two cortical BOLD time series, such as 1 radian, would correspond to a ~14-second time-lag between the time series and so forth.

Temporal reconstruction of complex PCs. To examine the temporal progression of each complex PC, we sampled the reconstructed BOLD time courses from each complex PC at multiple, equally spaced phases of its cycle (n = 30; Fig. 2). For each complex PC, the reconstruction procedure was as follows: (1) the complex PC time series was projected back into the original vertex-by-time space to produce time courses of the complex PC at each vertex; (2) the temporal phase of the complex PC was resampled into wavelet-transformed waveforms (repeating a full oscillation of the spatiotemporal pattern 0–2 pi radians); and (3) the vertex values within each bin were averaged to produce a ‘snapshot’ of BOLD activity at each phase bin (n = 30) of the spatiotemporal pattern. The end result is a spatiotemporal representation of each complex PC in terms of time-varying BOLD activity at equally spaced phases of its cycle.

Traveling index of complex PCs. The real and imaginary parts of a complex PC correspond to the spatial weights of the component at zero and pi/2 (90°) phase shift of the original time courses. In a sense, they encode the temporal evolution of the complex PC from one configuration (the real part) to a subsequent configuration (the imaginary part). By definition, a pure standing wave would exhibit the same spatial configuration from zero to pi/2 (90°) phaseshifts of its cycle. A pure traveling wave would exhibit a different spatial configuration from zero to pi/2 (90°) phaseshifts of its cycle. This observation suggests a means to quantify the degree of ‘traveling’ wave behavior of a complex PC using the statistical dependence between its real and imaginary parts. A coherent traveling wave (that is, propagation) of BOLD amplitudes across the cortex would exhibit one spatial configuration at one point in time and a different spatial configuration at another point in time. Thus, a complex PC that encodes this traveling wave behavior would exhibit differing spatial configurations in its real and imaginary spatial weights. Using a metric developed by Feeny\(^{54}\), we define the ‘traveling’ index of a complex PC as the reciprocal of the condition number of the matrix whose columns are the real and imaginary parts of the complex PC. This index completely encodes the statistical dependence between the real and imaginary parts of the complex PC. Pure traveling waves would exhibit completely orthogonal real and imaginary parts and a traveling index of one. Pure standing waves would exhibit completely dependent real and imaginary parts and a traveling index of zero.

Analysis of null models. We performed two null model exercises to determine the statistical properties of the cortical BOLD time courses that are necessary to capture the time-lag structure of the complex PCs. Null models allow the selective removal of features of the time courses, such as removing autocorrelation structure and preserving zero-lag correlation structure. First, to illustrate that the spatiotemporal patterns depend on properties of the time courses beyond zero-lag correlation, we randomly shuffled the timepoints of the time courses; this procedure selectively preserves the zero-lag correlation structure of spontaneous BOLD fluctuations and removes the time-lag (autocorrelation) structure. We randomly shuffled the group-concatenated BOLD time courses and estimated three complex PCs from cPCA. Second, we simulated time courses from a first-order multivariate autoregression model—that is, VAR(1)—that was fit to the cortical BOLD time series. A VAR(1) model predicts each time course from preceding timepoints (lag of one timepoint) itself and all other time courses (that is, all cortical vertices—4,800 time points). This model leaves the time-lag (that is, autoregressive) structure of the cortical BOLD time courses intact while assuming Gaussianity, linearity and stationarity of the time courses\(^{55}\). Due to the large number (4,800 cortical vertices) of highly collinear time courses, we extracted 200 dimension-reduced time courses from the original time courses using PCA. The VAR(1) model was fitted on the PC time courses, and simulated time courses (the same length as the original time courses) were generated from the fitted model. The simulated PC time courses were then filtered into the original cortical vertex space. CPCA was then applied to these simulated time courses.

Zero-lag FC analyses. Description of zero-lag FC analyses. Following the standard terminology of the fMRI literature, we refer to zero-lag synchrony among intrinsic
BOLD fluctuations as functional connectivity (FC).

FC between cortical brain regions organize into global, cortex-wide patterns, referred to as ‘FC topographies’. All analyses were conducted so as to be as consistent as possible with previous studies. For some of these analyses, results were compared with and without global signal regression. Global signal regression was performed by regression of the global mean time series (averaged across all cortical vertices) on all cortical time series. Residual time series from each regression were then used for subsequent analysis. All analyses were conducted using custom Python scripts and are publicly available at https://github.com/tsb46/BOLD_WAVES. The following zero-lag FC analyses were conducted:

- **PCA:** consists of eigendecomposition of the empirical covariance matrix of the vertices’ time series or, alternatively, SVd of the mean-centered group data matrix (time series along rows, vertices as columns). The first T PCs represent the top T dimensions of variance among cortical BOLD time courses. By construction, the first PC is the latent direction of variation with the largest explained variance across all input variables; it is followed by the second most explanatory component and so forth. The PC spatial weights on each vertex were used to interpret the spatial patterns of each PC. PC scores were obtained from the projection of the temporally concatenated group time series onto the PC space and represent the time course of each PC.

- **Varimax rotation of PCs:** consists of an orthogonal rotation of the PC spatial weights, such that the simple structure of the spatial weights are maximized. Simple structure is defined such that each vertex loads most strongly one component and weakly on all others. We adapted code from the Python package scikit-learn to perform varimax rotation.

- **LEs (spectral embedding):** a non-linear manifold learning algorithm popular in the FC gradient literature. The input to the LE algorithm was the vertex-by-vertex cosine similarity matrix, representing the similarity in the BOLD time series among all cortical vertices. Of note, cosine similarity is equivalent to Pearson correlation in mean-centered and unit-normalized time series (that is, T score normalization). We did not assume or try to derive a single ‘best’ number of latent dimensions to represent intrinsic functional brain organization. As we were interested in large-scale cortical patterns of FC, our survey focuses on low-dimensional latent solutions. As an initial estimate of the number of latent dimensions for all choices of dimension-reduction algorithms, we examined the first T PCs (where T was the dimensionality of interest) and the proportion of variance explained by the discarded components. This spatial outline was used to ensure that the seeds were placed within their appropriate location in the network. In addition, we also tested the robustness of our results for different seed locations in the three networks—medial insula (SMLV), inferior parietal cortex (DMN) and dorso-lateral prefrontal cortex (FPN)—and found that the results were identical.

- **CAP analysis:** Three CAP analyses were performed for the same three seed regions used in the seed-based regression analysis. CAP analyses first identify time-lag associations between all other brain regions. Consistent with previous studies, we chose the top 15% of timespans from the seed time course. The BOLD values for all cortical vertices in the top 15% timespans were then input to a-k means clustering algorithm to identify recurring CAPs of BOLD activity. We chose a two-cluster solution for all CAP analyses. For each seed, the two clusters were labeled as the ‘active’ and ‘de-activations, somewhat similar to CAPs. To avoid overfitting and to reduce noise in the high-dimensional input data, we conducted a PCA of the cortical BOLD time series. The first 100 PC projections of the time series served as input to the HMM algorithm. Associated with each brain state is a mean amplitude vector with a value for each PC (n = 100) and a covariance matrix between the 100 PC components. The mean amplitude vector represents the pattern of BOLD activity amplitudes associated with that brain state. For interpretation, the mean amplitude vector is projected back into cortical vertex space for interpretation. A variety of potential ‘observation models’ are frequently used in HMM models. As cortical time series are measured on a continuous scale (as opposed to discrete measurements), the probability of a timepoint conditional on a given brain state (the emission probability) is modeled as a mixture of Gaussian distributions. We used the HMM algorithm with Gaussian mixture emission probabilities implemented in the Python package hmmlearn (https://github.com/hmmlearn/hmmlearn).

- **Modularity analysis:** To determine whether the community structure of cortical BOLD time courses can be explained by the three spatiotemporal patterns, we applied the Louvain modularity maximization algorithm to the original FC matrix and an FC matrix reconstructed from the three spatiotemporal patterns. FC matrices were calculated by computing the Pearson correlation coefficient between all pairs of cortical vertex time courses. The reconstructed FC matrices were created from projecting the time courses of the top 15% PCs back on to vertex space and computing an FC matrix. The Louvain modularity maximization algorithm was applied with a resolution parameter value of 1 (with asymmetric treatment of negative weights). To compare the degree of similarity between the community structure of the original and reconstructed FC matrix, we computed the NMI between their community assignments from the Louvain algorithm. The NMI varies from 0 (completely independent communities) to 1 (completely identical communities). This analysis was performed using the Python package bcipy (https://github.com/aestrivex/bcipy).

**Model selection:** choice of number of dimensions in dimension-reduction algorithms.

The dimension-reduction algorithms used in this study, including PCA, PCA with varimax rotation, spatial and temporal ICA and LE, as well as HMMs, require a choice of the number of latent dimensions/hide states to estimate. For PCA with varimax rotation, spatial and temporal ICA and HMM, this controls the degree of richness and/or fine-grained distinctions of the data description—that is, how many separate unobserved hidden phenomena are assumed and quantitatively modeled to underlie each given data point or observation. We did not assume or try to derive a single ‘best’ number of latent dimensions to represent intrinsic functional brain organization. As we were interested in large-scale cortical patterns of FC, our survey focuses on low-dimensional latent solutions. As an initial estimate of the number of latent dimensions for all choices of dimension-reduction algorithms, we examined the first T PCs (where T was the dimensionality of interest) and the proportion of variance explained by the discarded components. This spatial outline was used to ensure that the seeds were placed within their appropriate location in the network. In addition, we also tested the robustness of our results for different seed locations in the three networks—medial insula (SMLV), inferior parietal cortex (DMN) and dorso-lateral prefrontal cortex (FPN)—and found the same elbow after three components in a scree plot constructed from the three networks.

**QPP and lag projections.** There are two widely used algorithms for the study of spatiotemporal patterns in BOLD signals: (1) interpolated cross-covariance functions (Mitra et al.26,27) for the detection of lag/latency projections (~0–2 seconds) and (2) a repeated-template-averaging algorithm of similar spatiotemporal segments for detection of the QPP (~20 seconds).

Lag projections represent the average time-lag between a brain regions time course and that of another brain region. This provides an estimate of the average temporal ‘ordering’ of brain region time courses, such that a brain region with a greater average time-lag occurs after a brain region with a smaller average time-lag.

For our study, we applied the lag projection algorithm to all cortical vertex time courses. The time-lag between a pair of cortical vertex time courses is defined as the time-lag that maximizes the cross-correlation function. Lagged projections are defined as the column average of the pair-wise time-lag matrix between all cortical vertex time courses. An analogous column-wise averaging operation can be applied to the complex correlation matrix used by CPCa. Specifically, we computed the column-wise circular mean of the pair-wise phase delay values of the complex...
correlation matrix. The circular mean was computed due to the circular nature of the phase values of a complex correlation (that is, \(-pi\) and \(pi\) are identical phase differences).

To estimate the QPP, the template autoregressive matching algorithm of Majeed et al.\(^{18}\) was used. The algorithm operates in the following manner. Start with a random window of BOLD timepoints, compute a sliding window correlation of the window across the temporally concatenated group data at each timepoint and then average this segment with similar segments of BOLD timepoints (defined using a correlation threshold). This process is repeated iteratively until a level of convergence is reached. The result is a spatiotemporal averaged template of BOLD dynamics (that could be displayed in a movie, for example), along with the final sliding window correlation time series. The final sliding window time series is the same length as the original participant or group concatenated time series and provides a time index of the appearance of the QPP in BOLD data. Python code for this analysis was modified from the C-PAC toolbox (https://hcp-indi.github.io/). Consistent with previous studies\(^{18,28}\), the following parameters were chosen for the template matching algorithm: the window length was 30 TRs; the maximum correlation threshold for identifying similar segments was \(r > 0.2\); and the algorithm was repeated ten times. The template with the highest average sliding window correlation time series across the ten runs was chosen as the final result.

**Statistics and reproducibility.** No calculations were used to predetermine sample size. It is important to note that this analysis was conducted at the within-participant level, with 1,200 sampled timepoints per participant. Thus, the true ‘sample size’ was substantially larger than 50 data points. Our analyses suggest that \(n = 50\) is sufficient to replicate the three spatiotemporal patterns across independent samples. No experimental conditions were randomized. No data were excluded from analysis. The investigators were not blinded to allocation during experiments and outcome assessment.

**Reporting summary.** Further information on research design is available in the Nature Research Reporting Summary linked to this article.

**Data availability**

Data from the Human Connectome Project (HCP) are publicly available at http://www.humanconnectomeproject.org/data/. Instructions for accessing HCP data can be found at https://www.humanconnectome.org/. All metadata are provided at https://github.com/tsb46/BOLD_WAVES.

**Code availability**

All code for pre-processing and analysis is provided at https://github.com/tsb46/BOLD_WAVES.

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**Author contributions**

T.B. performed all analyses. S.D.K developed the original QPP algorithm used in this study. L.Q.U., S.D.K., B.T.T.Y., J.N. and C.C assisted in the interpretation of analyses, conceptualization of the project and writing of the manuscript. J.S. assisted in the development and testing of the publicly available GitHub repository that documents and stores analysis code.

**Competing interests**

The authors declare no competing interests.

**Additional information**

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Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection: No software was used for data collection.

Data analysis: All metadata and analysis code is provided at https://github.com/tsb46/BOLD_WAVES.
- Visualization and Pre-processing Software: Connectome Workbench (V1.4.2.)
- Analysis Python Packages: fbpca (V1.0), scikit-learn (V1.0.2), xmca (V1.4.2), hmmlearn (V0.2.7), statsmodels (0.12.1)

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Data from the Human Connectome Project (HCP) is publicly available at http://www.humanconnectomeproject.org/data/. Instructions for accessing HCP data can be found at https://www.humanconnectome.org/. All metadata is provided at https://github.com/tsb46/BOLD_WAVES.
Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender

The main sample consisted of 21 males and 29 females. The replication sample consisted of 22 males and 28 females. Results were analyzed across both sexes, and not split by sex. As our interest was population-level BOLD patterns, we did not consider differences by sex.

Population characteristics

The Human Connectome project sample was a population of adults (N=1200; ages 22-37) from the surrounding St. Louis, MI area. We chose a random subset of this large sample (N = 50), and another random subset as a replication dataset (N=50).

Recruitment

Details can be found in Van Essen DC, Smith SM, Barch DM, Behrens TE, Yacoub E, Ugurbil K; WU-Minn HCP Consortium. The WU-Minn Human Connectome Project: an overview. Neuroimage. 2013 Oct 15;80:62-79. doi: 10.1016/j.neuroimage.2013.05.041. Epub 2013 May 16. PMID: 23684880; PMCID: PMC3724347.

Ethics oversight

Informed consent was obtained from all subjects. All methods were carried out in accordance with relevant guidelines and the University of Miami Institutional Review Board approved the study.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

- Life sciences
- Behavioural & social sciences
- Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

| Sample size | N = 50 for study sample, N = 50 for replication sample. No a priori calculations were used to predetermine sample size. It is important to note that this analysis was conducted at the within-subject level, with 1200 sampled time points per subject. Thus, the true 'sample size' was substantially larger than than 50 data points. Our analyses suggests that N=50 is sufficient to replicate the three spatiotemporal patterns across independent samples. |
| Data exclusions | No data exclusions |
| Replication | Replication sample (N=50) was used to assess robustness of findings. All replication attempts were successful. |
| Randomization | No randomization of experimental conditions was implemented. The authors only analyzed one experimental condition - resting-state. |
| Blinding | No treatment vs. control group comparisons were conducted in our analyses. Our analysis consisted of one experimental condition: resting-state. There was no need to blind researchers to the allocation of a single experimental condition. |

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

| n/a | Involved in the study |
| --- | --- |
| n/a | Antibodies |
| n/a | Eukaryotic cell lines |
| n/a | Palaeontology and archaeology |
| n/a | Animals and other organisms |
| n/a | Clinical data |
| n/a | Dual use research of concern |

Methods

| n/a | Involved in the study |
| --- | --- |
| n/a | ChIP-seq |
| n/a | Flow cytometry |
| n/a | MRI-based neuroimaging |
# Magnetic resonance imaging

## Experimental design

| Design type | Resting-state |
|-------------|---------------|
| Design specifications | 15min resting-state scans - eyes open with white fixation cross |
| Behavioral performance measures | None |

## Acquisition

| Imaging type(s) | Functional |
| Field strength | 3T |
| Sequence & imaging parameters | Multi-band Gradient Echo EPI, TR=0.72s, TE = 33.1ms, 2mm Isotropic spatial resolution |
| Area of acquisition | Whole Brain |
| Diffusion MRI | Not used |

## Preprocessing

| Preprocessing software | Connectome Workbench; and custom Python scripts |
| Normalization | Surface normalization to standard grayordinates space. Details at: Glasser MF, Sotiropoulos SN, Wilson JA, Coalson TS, Fischl B, Andersson JL, Xu J, Jbabdi S, Webster M, Polimeni JR, Van Essen DC, Jenkinson M; WU-Minn HCP Consortium. The minimal preprocessing pipelines for the Human Connectome Project. Neuroimage. 2013 Oct 15;80:105-24. doi: 10.1016/j.neuroimage.2013.04.127. Epub 2013 May 11. PMID: 23668970; PMCID: PMC3720813. |
| Normalization template | Conte64 surface template |
| Noise and artifact removal | Functional scans went through ICA-based artifact removal (ICA-FIX) described in: Smith, S. M., Beckmann, C. F., Andersson, J., Auerbach, E. J., Bijsterbosch, J., Douaud, G., Duff, E., Feinberg, D. A., Griffanti, L., Harms, M. P., Kelly, M., Laumann, T., Miller, K. L., Moeller, S., Petersen, S., Power, J., Salimi-Khorshidi, G., Snyder, A. Z., Vu, A. T., Woolrich, M. W., ... WU-Minn HCP Consortium (2013). Resting-state fMRI in the Human Connectome Project. Neuroimage, 80, 144–168. https://doi.org/10.1016/j.neuroimage.2013.05.039 |
| Volume censoring | None |

## Statistical modeling & inference

| Model type and settings | A first-order multivariate autoregressive model (VAR(1)) was used as a null model simulation. The VAR(1) model was fit to the empirical (BOLD) time courses, and simulated time courses were generated from this fitted model. These simulated time series were analyzed to assess whether the empirical spatiotemporal patterns were consistent with a stochastic, stationary time series process. |
| Effect(s) tested | Spatial maps and time-series were compared using the Pearson correlation coefficient |
| Specify type of analysis: | Whole brain | ROI-based | Both |
| Statistic type for inference | No statistical inference was performed at a voxel-level. |
| Correction | Analyses were exploratory and aimed to compare outputs of different analyses. No multiple comparison corrections were performed. All analyses were replicated in an independent sample. |

## Models & analysis

| n/a | Involved in the study |
| --- | --- |
| ☒ ☒ | Functional and/or effective connectivity |
| ☒ ☒ | Graph analysis |
| ☒ ☒ | Multivariate modeling or predictive analysis |
| Functional and/or effective connectivity | Functional connectivity is a broad term that may refer to host of different analysis methods - a primary aim of our paper was to compare the outputs of a large variety of functional connectivity methods |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Graph analysis                          | Graphs were constructed from Pearson correlations between whole-brain surface vertices. Community detection was performed using the Louvain modularity algorithm.                                                                                          |
| Multivariate modeling and predictive analysis | A wide-variety of exploratory dimension-reduction and clustering algorithms were used.                                                                                                           |