Segment-Then-Connect: Change Point Dynamic Connectivity for Early MCI Detection

Anonymous Author(s)
Affiliation
Address
email

Abstract

The most widely used inputs in classification models for resting-state functional magnetic resonance imaging (rs-fMRI) data are estimates of static-based functional connectivity (SFC) and sliding window dynamic functional connectivity (swDFC). Although these methods are computationally convenient, the resulting representations are highly simplified portrayals of a deeply integrated and dynamic process. Change point dynamic functional connectivity (cpDFC) methods offer an alternative to swDFC approaches with many advantages. In this study, we consider a classification task between controls and patients with eMCI using rs-fMRI data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) studies, ADNI2 and ADNIGO. Our results indicate that the DFC methods are generally superior to the SFC methods when used as inputs into the classification model. Most importantly, we find that cpDFC is generally superior to swDFC. We discuss how cpDFC methods offer greater parsimony of network features and ease of interpretability. Our empirical results indicate that functional brain network representations are dynamic, multiscale, and subject-specific, underscoring the need for a learning paradigm tailored to these properties.

1 Introduction

Resting-state functional magnetic resonance imaging (rs-fMRI) enables the investigation of brain connectivity without task-related variability, making it useful for detecting functional differences in neurological conditions [Biswal et al., 1995]. Functional connectivity (FC) quantifies statistical dependencies between regions of interest (ROIs) and is often represented as a graph [Muldoon and Bassett, 2016, Bassett and Bullmore, 2017]. While static FC (SFC) assumes constant connectivity, dynamic FC (DFC) captures time-varying interactions that better reflect neural processes [Hutchison et al., 2013]. The sliding-window approach (swDFC) is by far the most common method for DFC [Allen et al., 2014], but suffers from arbitrary window-size selection, redundancy from overlapping windows, and assumptions about uniform change rates [Zalesky and Breakspear, 2015, Leonardi and Van De Ville, 2015]. Furthermore, rs-fMRI time series are known to exhibit discrete state-switching rather than smooth, continuous drifts as assumed in swDFC [Allen et al., 2014].

We propose a segmentation-first approach that aligns more closely with the true generative process. Change point dynamic functional connectivity (cpDFC), which segments fMRI time series into non-overlapping stationary intervals in a data-driven manner. This approach reduces redundancy, captures subject-specific dynamics, and can produce more discriminative features for disease classification. We evaluated cpDFC against SFC and swDFC in distinguishing early mild cognitive impairment (eMCI) from healthy controls using Alzheimer's Disease Neuroimaging Initiative (ADNI) rs-fMRI data, and validated on an independent MCI dataset [Mascali et al., 2015]. Our work tackles key challenges in neuroimaging, namely, modeling complex, high-dimensional time series data (rs-fMRI),

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capturing distributional shifts, and generating interpretable, reliable representations for clinical classification. Unlike fixed-window approaches that impose uniform temporal segmentation, cpDFC adaptively discovers subject-specific, stationary network regimes, parsing meso-scale dynamics that may correspond to evolving cognitive states or neural processes. Using change points, our approach instead extracts structured, meaningful segments that are more amenable to clinical deployment.

Our contributions are as follows: (1) the first application of change point detection to classify neurodegenerative diseases from rs-fMRI, (2) a systematic comparison of cpDFC, swDFC, and SFC, including step-size effects of swDFC, (3) the demonstration that cpDFC produces superior accuracy and interpretability, (4) evidence that combining multiple FC methods in an ensemble improves performance for eMCI classification and provides richer representations than any one method.

2 Methods

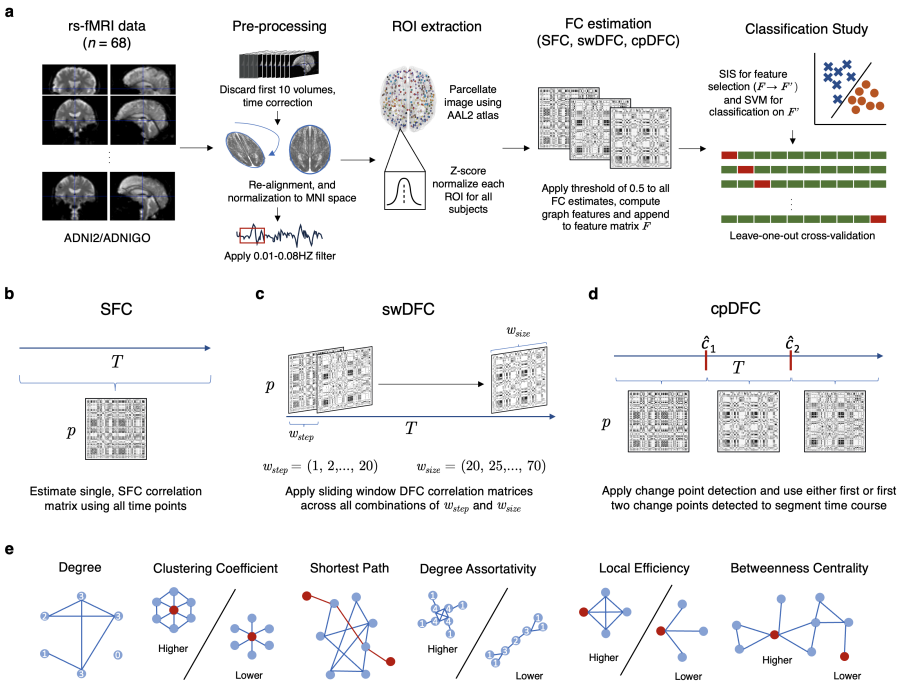

Figure 1: A schematic of CN/eMCI classification task starting from raw rs-fMRI data to eMCI/control classification for the ADNI rs-fMRI dataset. Panel (a) is the overall pipeline, while panels (b), (c), and (d) show the different FC methodologies (SFC, swDFC, cpDFC, respectively). Panel, (e), shows example graphs expressing the topological features used in the classification study.

We provide notation in the Supplementary Materials A. In ADNI's rs-fMRI dataset, we analyzed 33 subjects with early mild cognitive impairment (eMCI; mean age 72.3, 15M/18F) and 35 healthy controls (mean age 74.6, 14M/21F). Data were preprocessed in SPM [SPM, 2023] following a standard fMRI pipeline, including removal of initial volumes, motion correction, spatial normalization to MNI space, nuisance regression, spatial smoothing, detrending, and band-pass filtering (0.01–0.08 Hz). The brain was parcellated into 120 regions using the AAL2 atlas [Tzourio-Mazoyer et al., 2002], and Z-score normalized. The final data set of each subject was a $T = 130$ by $p = 120$ matrix (time points $\times$ ROIs). Full details are provided in the Supplementary Materials C.

For each stationary segment $\boldsymbol{S}$, FC between ROIs i and j is estimated using Pearson's correlation ρ_{ij}. An edge is kept if $|\rho_{ij}| > 0.5$, which yields graphs of strong statistical dependence [Adamovich et al., 2022]. For each subject, SFC assumes one stationary segment (entire scan), whereas DFC yields multiple segments. We estimate DFC under the assumption of unknown distributional shifts and rate of change, but with stationary segments existing in $\boldsymbol{X}$. Two approaches were used:

Sliding windows (swDFC): a fixed-length window (w) is shifted by step size (s), with FC computed in each (Algorithm 1 in Supplementary Materials; schematic in Figure 1c).

Change points (cpDFC): we use FaBiSearch [Ondrus et al., 2025], which detects multiple change points in multivariate time series based on network structure via non-negative matrix factorization [Lee and Seung, 1999]. The hyperparameters $(\delta, n_{\text{run}}, n_{\text{reps}})$ are established using recommendations from Ondrus and Cribben [2024]. Change points are ordered by p-value, and the first $k = 1$ or $k = 2$ are used to segment the time series before FC estimation. We also test NCPD [Cribben and Yu, 2017] and CRMT [Ryan and Killick, 2023] with comparable settings.

For each segment's graph, we compute standard node- and network-level metrics, degree, clustering coefficient, shortest path length, degree assortativity, local efficiency, and betweenness centrality, as candidate features [Rubinov and Sporns, 2010]. Formal definitions are provided in the Supplementary Materials G.

Labels are defined as $c = 0$ (control) and $c = 1$ (eMCI). The features of all segments are concatenated, and sure independence screening (SIS; Fan and Lv, 2008) selects a reduced set $\boldsymbol{F}'$. We train a linear SVM [Boser et al., 1992], chosen for robustness after testing RBF-SVM, logistic regression, and decision trees. We compare SFC, swDFC, and cpDFC in separate experiments. For SFC, all $T = 130$ time points are used. For swDFC, we test $w \in [10, 70]$ (step 5) and $s \in \{1, 2, 3, 5, 8, 10, 15, 20\}$. For cpDFC, we evaluate FBS_cpDFC1 and FBS_cpDFC2. SIS and SVM are applied within each fold of leave-one-out cross-validation (68 subjects total). The complete pipeline is shown in Figure 1a.

3 Results

We first evaluate SFC, swDFC, and cpDFC separately, and then combine the best-performing models in an ensemble. Figure 2 summarizes the results. For swDFC, we report only window/step size combinations achieving accuracy $\geq 63.57\%$ (one standard error above the null accuracy of 51.47%). Among all methods, FBS_cpDFC2 achieves the highest overall performance in two of four metrics: accuracy 77.94%, F1 80.00%, sensitivity 90.91%, and specificity 65.71%. The only metric in which FBS_cpDFC2 is significantly different from swDFC is sensitivity, but the two swDFC variants with higher sensitivity (60w_15s and 70w_10s) perform notably worse in other metrics. Compared to the best swDFC configuration (15w_3s: accuracy 72.06%, F1 74.67%), FBS_cpDFC2 performs slightly better (n.s., $p = 0.250$) but is significantly superior compared to the full swDFC set ($\mu = 0.5852$, $\sigma = 0.0483$; all metrics $p < 1.4 \times 10^{-5}$). cpDFC1 and SFC both underperform, with SFC near null accuracy. Across all (w, s) combinations of swDFC (Supplementary Materials B.1), no performance trend emerges and small parameter changes can cause large accuracy drops.

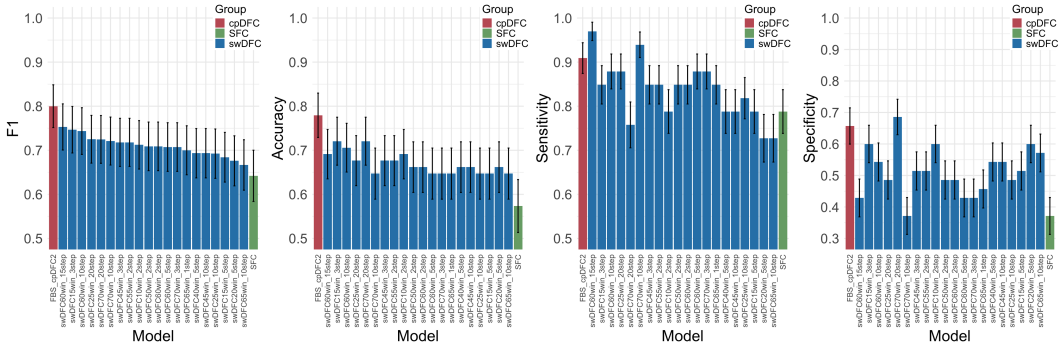

Figure 2: F1, accuracy, sensitivity, and specificity results from the classification study of CN subjects and subjects with eMCI in the ADNI rs-fMRI dataset. SFC, cpDFC, and swDFC correspond to static, change point, and window based dynamic functional connectivity, respectively.

In general, the difference between FBS_cpDFC2 and the best swDFC combination ($w = 60$, $s = 15$) can be summarized as such: F1 score improved by 6.26%, accuracy by 12.76%, and specificity by 53.31%, while the sensitivity was lower by 6.25%. swDFC exhibited substantial variability, depending on the choice of window and step sizes, with accuracy in the range of $22.06\% - 72.06\%$, F1 score $19.35\% - 75.29\%$, sensitivity $18.18\% - 96.97\%$, and specificity $14.29\% - 68.57\%$.

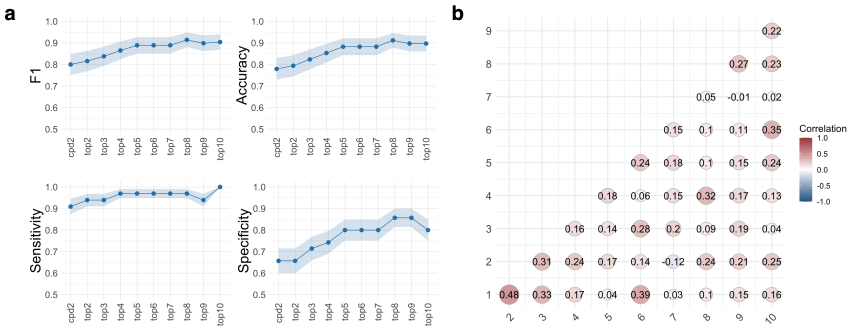

Figure 3: The ensemble model results from the classification study of CN subjects and subjects with eMCI in the ADNI dataset. Panel (a) shows the ensemble results, which combines the predictions from the top-2 to the top-10 classifier models as determined by F1 score. FBS_cpDFC2 is the best stand-alone classifier. Shaded regions indicate $\pm$ the standard error of proportion calculated. (b) shows the correlation between predicted probabilities of eMCI across the top-10 classifiers.

Figure 3 shows the performance of the ensemble when combining predictions from the top-2 to top-10 classifiers (ranked by F1 score). The best single model is FBS_cpDFC2. Combining additional models does yield an improvement, likely due to minimal overlap in predictive information and differences in assumed rates of change. A correlation of predicted probabilities (Figure 3b) shows significant correlations (p-value = $4.00e-5$ and $1.09e-3$, respectively, t-test, $\alpha < 0.05$, adjusted for multiple comparisons using Benjamini and Hochberg, 1995) between cpDFC2 and two swDFC variants (swDFC40w_5s, swDFC35w_20s), indicating redundancy between these feature spaces.

4 Discussion

Our results show that subject-specific temporal segmentation via change point DFC via FBS_cpDFC2, yields the strongest and most stable eMCI classification performance in ADNI rs-fMRI. Although the locations of the change points vary widely between individuals, the rate of change itself is not directly discriminative; instead, cpDFC's advantage comes from capturing individualized temporal dynamics without imposing fixed window parameters. Across the entire grid, swDFC shows high variability, occasional performance below SFC, and unstable feature selection, underscoring the risks of exhaustive parameter search and multiple hypothesis testing. Furthermore, cpDFC achieves these results with 33% fewer selected features (28 vs. 42) and without costly hyperparameter tuning, making it less prone to overfitting than swDFC in small-sample, high-dimensional settings.

Post-hoc ensemble analysis combining the best models yields further gains, supporting the idea that multi-timescale information improves classification. Significant correlations between some model predictions indicate partial redundancy, but diverse temporal scales still provide complementary features. Performance gains plateau after the top-8 ensemble, suggesting diminishing returns. Replication on an independent MCI dataset (Supplementary Materials C.2) confirmed the superior performance of cpDFC over all swDFC variants, despite differences in acquisition and preprocessing, suggesting robustness to dataset-specific factors.

Overall, our findings suggest: (1) individualized temporal segmentation is more robust than fixed-window approaches; (2) change point detection offers a principled alternative to swDFC for dynamic FC estimation; and (3) integrating multiple temporal resolutions can capture complementary neural dynamics for downstream tasks. Our cpDFC approach exemplifies a data-driven, segmentation-first approach that circumvents the need to tune hyperparameters such as window size, enabling stable, interpretable features from high-dimensional brain signals. Our ensemble findings highlight how multi-timescale fusion can enhance classification by aggregating complementary information.

We acknowledge that our work has some limitations. One is that the smaller sample size ($n = 68$) may limit the ability to generalize to larger populations, particularly given the heterogeneity of eMCI. Additionally, our study uses some fixed pre-processing and parcellation choices which could influence downstream classification. Future works could explore larger studies and jointly learn segment boundaries and within-segment representations end-to-end using deep-learning approaches.

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A Notation

We denote a matrix with a bold capital letter $\boldsymbol{A}$ and vectors as bold lowercase letters $\boldsymbol{a}$. The entry corresponding to the ith row and the jth column in $\boldsymbol{A}$ is $\boldsymbol{A}_{ij}$. The vector of the ith column in $\boldsymbol{A}$ is given by $\boldsymbol{A}_i$. We denote a single subject's fMRI data by $\boldsymbol{X}$, where each data matrix $\boldsymbol{X} \in \mathbb{R}^{T \times p}$ has T time points and p ROIs. A time point t is an element of the time index set $\{1, \ldots, T\}$. A stationary segment in $\boldsymbol{X}$ is denoted by $\boldsymbol{S} = \{x_t \in \mathbb{R}^p : t_1 \leq t \leq t_2\}$ where $t_1, t_2 \in \{1, \ldots, T\}$. A graph $\mathcal{G}$ is defined as a collection of vertices and edges $\mathcal{G} = (V, E)$. We use the terms "graph" and "network" interchangeably throughout. The number of samples or subjects in each study is denoted by n.

B Additional results

B.1 Sliding window results

Figure 4 shows the results of different combinations of window size and step size for swDFC. Across the various combinations, there is no clear relationship between step size and window size. Additionally, there are several combinations that are plagued by instability, as shown by the large variability in step and window sizes in neighboring combinations (or tiles). For example, the combination of window size 15 and step size 3 achieved the best accuracy of 72.06%. However, changing the window size by 5 time points in either direction (to either 10 or 20), drastically reduces the performance of these models (to 58.82% and 55.88%, respectively). The same is also evident when the step size is changed to 2 or 8: the performance of the models reduces to 52.94% and 64.71%, respectively.

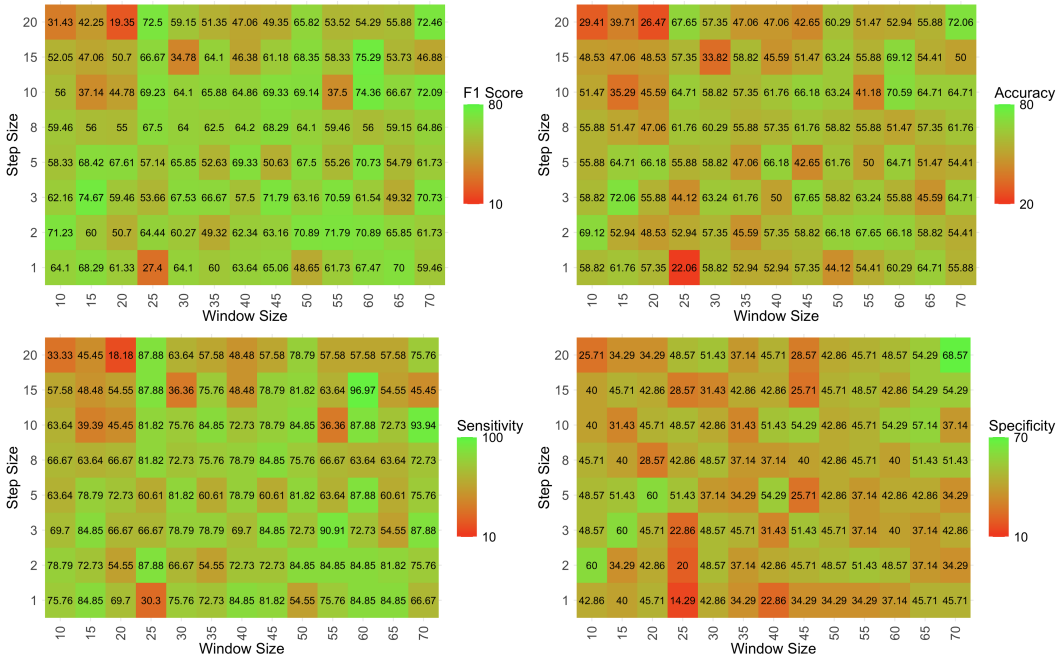

Figure 4: Heatmaps of F1 score, accuracy, sensitivity, and specificity from the classification study of CN subjects and subjects with eMCI from the ADNI rs-fMRI dataset using swDFC. Results are shown across window sizes [10, 70] in increments of 5 and step sizes [1, 2, 3, 5, 8, 10, 15, 20].

Figure 4 shows the results of different combinations of window size and step size for swDFC. Across the various combinations, there is no clear relationship between step size and window size. Additionally, there are several combinations that are plagued by instability, as shown by the large variability in step and window sizes in neighboring combinations (or tiles). For example, the combination of window size 15 and step size 3 achieved the best accuracy of 72.06%. However, changing the window size by 5 time points in either direction (to either 10 or 20), drastically reduces

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B.2 Secondary dataset

We present the classification results from the Mascali et al. [2015] dataset. We also include two additional change point detection methodologies, specifically Network Change Point Detection (NCPD: Cribben and Yu, 2017) and Covariance Change Points through Random Matrix Theory (CRMT: Ryan and Killick, 2023). Figure 5 (top panel) shows the classification results using SFC, swDFC and cpDFC methods. Similar to the ADNI data set, FaBiSearch with two change points has a superior performance compared to the other methods. In addition, it appears that change point methods outperform swDFC methods. In Figure 5 (bottom panels), we again find that there is no particular patterns between the different combinations of step size and window size and classification performance. The best performing models have a window size of approximately 40 and step size between 5 and 20 depending on the evaluation metric. For swDFC, performance on this dataset mirrors ADNI but is often inferior. Given the smaller size of this study ($n = 20$) compared to the ADNI data set ($n = 68$), it is possible that the performance discrepancies between the combinations of window and step size are further exacerbated in smaller sample size settings. Figure 6(a) shows the ensemble analysis for the Mascali et al. [2015] dataset. The lack of a monotonically increasing performance pattern as more models are combined may stem from the small sample size. Alternatively, it could be due to the larger number of higher correlations between the models (Figure 6(b)).

B.3 Change point detection and stationary segments

To estimate cpDFC, we apply FabiSearch [Ondrus et al., 2025] to each subject in the ADNI dataset. Figure 7 shows both the detected change points for the control group (CN) (Figure 7(a)) and the eMCI group (Figure 7(b)). Within each group, the change points are not consistently clustered around specific time points during the scan; rather, they are distributed relatively uniformly, aside from some edge effects near the start and end of the session. This observation suggests that the timing of change points is largely subject-specific, rather than being driven by a group-level pattern. A non-parametric Kolmogorov-Smirnov test on the change point locations between the two groups suggests that they are not significantly different ($p = 0.413$). A one-sided t-test on the means of the location of the first detected change points of the CN group and the eMCI groups suggests that the first change point for the CN group is significantly smaller (in time) than the eMCI group ($p = 0.028$).

Figure 7 also shows the stationary FC states (or modes) between each change point, where $\boldsymbol{S}_1, \boldsymbol{S}_2, \boldsymbol{S}_3$ refer to the first, second, and third stationary segments estimated by change point detection, respectively. Across all segments and even between the CN and subjects with eMCI, there is strong FC between the frontal and cerebellar regions. In the first FC state, $\boldsymbol{S}_1$, CN have stronger FC between the parietal regions and the rest of the brain, and also engage the temporal regions with the rest of the brain more as well. Subjects with eMCI, have stronger FC between the frontal and parietal regions.

In $\boldsymbol{S}_2$, CN subjects exhibit strong FC between the frontal and parietal regions. In contrast, subjects with eMCI show FC primarily concentrated in the frontal regions, with connections extending to the occipital and limbic systems. Notably, a small number of occipital nodes in subjects with eMCI mediate much of the FC to other brain regions. In $\boldsymbol{S}_3$, CN patients display robust FC among the frontal, occipital, and cerebellar regions, forming a tightly coupled triad. Conversely, subjects with eMCI exhibit more diffuse FC, with the cerebellum acting as a hub, extensively connected to the rest of the brain, particularly the parietal lobe.

B.4 Graph structure changes across time segments

In Figure 8(a), we show the ROIs that were selected by SIS in all folds in leave-one-out cross-validation for FBS_cpDFC2. Figure 8(b) includes more information on the selected features and the corresponding ROIs, such as node ID, feature type, stationary segment, and differences in the mean value for the features of the CN and the eMCI groups. We find that the most consistently chosen features correspond to the frontal, parietal, and cerebellum regions. Degree, betweenness, clustering coefficient, local efficiency, and shortest path were all key features that were selected across LOOCV folds. We also find that eMCI is associated with lower degree in the parietal region,

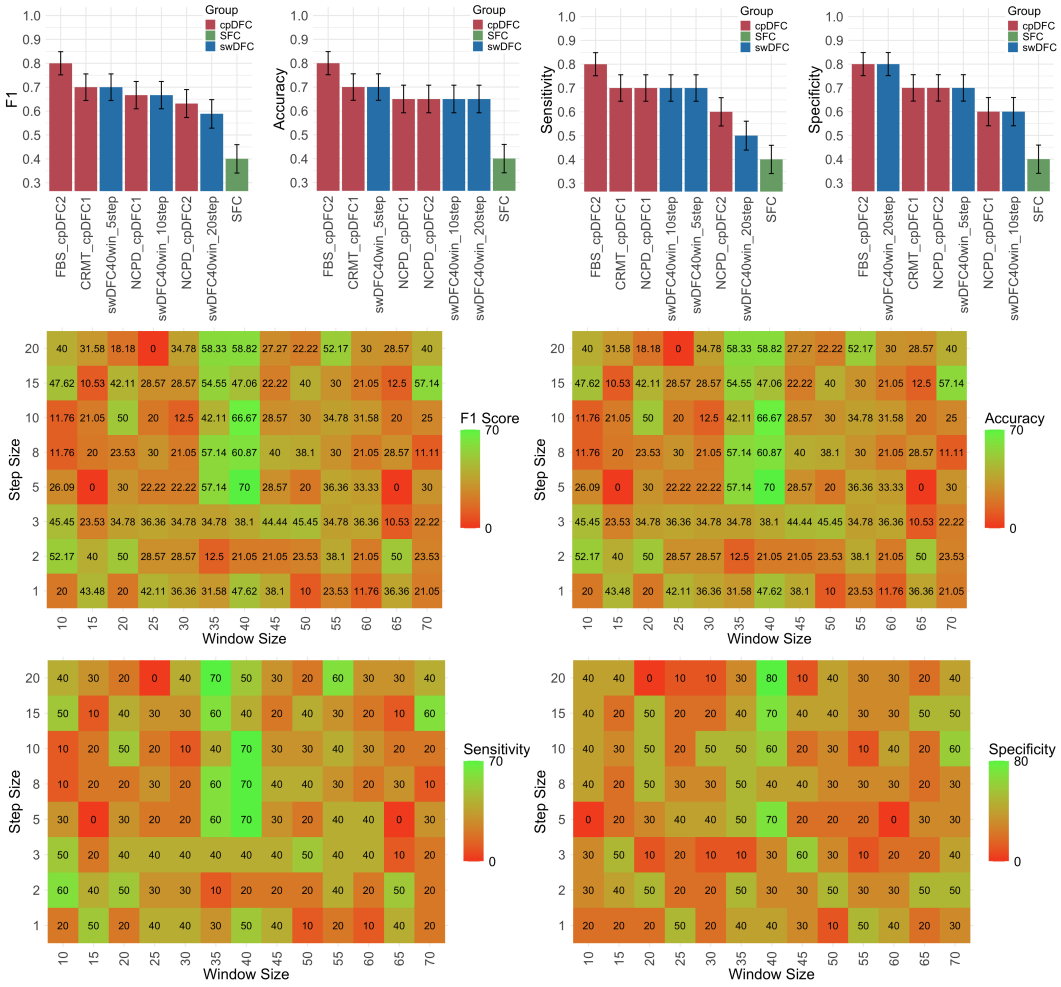


Figure 5: The classification results of CN subjects and subjects with MCI from the Mascali et al. [2015] rs-fMRI dataset. (Top panel) F1, accuracy, sensitivity, and specificity results of all methods. SFC, cpDFC, and swDFC correspond to static, change point, and window based dynamic functional connectivity, respectively. (Bottom panels) Heatmaps of F1 score, accuracy, sensitivity, and specificity. Results are shown across window sizes [10, 70] in increments of 5 and step sizes [1, 2, 3, 5, 8, 10, 15, 20].

and that paths were more efficient, shorter, and tightly clustered in the cerebellum and frontal regions. Later segments ($\boldsymbol{S}_2$, and $\boldsymbol{S}_3$) were chosen more often across these folds, which may be related to the subjects being more settled and closer to a true “resting" state compared to the beginning of the fMRI experiment.

As the results in the main article show, there is a concentration of strongly differentiating features in the later time segments (Figure 8) for the classification task. This is highlighted also in Figure 9, especially in the ROIs close to the main diagonal, and also in the squared difference row, which are the largest for time segments 2 and 3. It is evident that the group-wise characteristics become more stable and contribute most to the differentiation in later time windows. Furthermore, it is clear from Figure 9 that global changes in graph structure are subtle, since the averaged adjacency matrices are generally relatively similar, but localized differences in functional connectivity have widespread effects related to the global graph structure. For example, we observed differences in the shortest path metric, which can be strongly influenced by changes in one or a few edges, especially if there is a lack of redundancy in connections between nodes. Therefore, these subtle differences in the graph structure have strong consequences in distinguishing CN from patients with eMCI.

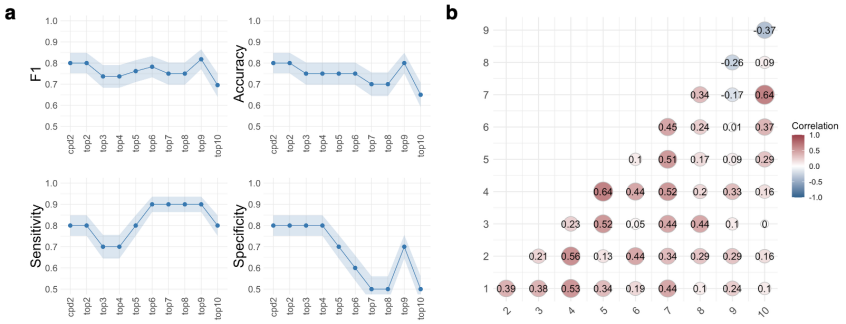


Figure 6: The ensemble model results from the classification study of CN subjects and subjects with eMCI in the Mascali et al. [2015] dataset. Panel (a) shows the ensemble results. For the ensemble model, we combined the predictions from the top-2 to the top-10 classifier models, as determined by their highest F1 score. The FBS_cpDFC2 model is the best stand-alone classifier. Shaded regions indicate $\pm$ the standard error of proportion calculated as $SE = \sqrt{\frac{\hat{p}(1-\hat{p})}{n}}$. (b) shows the correlation between predicted probabilities of eMCI across the top-10 classifiers, as determined by the highest F1 score.

As we restrict each subject to two change points, each subject has 3 stationary segments, or partitions between change points (or stationary modes). We can then compare group-wise differences in the adjacency matrices between consecutive segments. We calculate the average adjacency matrix for each segment and class (CN or eMCI), using the following procedure. For each group (CN: $n = 35$, eMCI: $n = 33$), $\mu \boldsymbol{A}_{ij} = \frac{1}{n} \sum_{k=1}^{n} \boldsymbol{A}_{ij}$. We can then calculate the entry-wise difference between the groups using $\mu \boldsymbol{A}^{\text{diff}} = \mu \boldsymbol{A}^{\text{CN}} - \mu \boldsymbol{A}^{\text{eMCI}}$. Figure 9 (rows 1 and 2) shows the average adjacency matrices grouped by segment (1, 2, or 3) and class (CN or eMCI), while Figure 9 (row 3) shows the differences in class between segments for all 120 ROIs. The differences appear to concentrate close to the diagonal of the adjacency matrices. This difference is especially pronounced between ROIs 50-60. In addition, subjects with eMCI have stronger off-diagonal connections, notably at the intersection of ROIs 10-20 and 80-90.

C Data and pre-processing

C.1 ADNI data

The first dataset we obtained from the ADNI database (`http://adni.loni.usc.edu`). ADNI was launched in 2003 as a public-private partnership, led by Principal Investigator Michael W. Weiner, MD. The primary objective of ADNI has been to test whether serial magnetic resonance imaging, positron emission tomography, other biological markers, and clinical and neuropsychological evaluations can be combined to measure the progression of MCI and early AD. For up-to-date information, see `www.adni-info.org`. In ADNI's rs-fMRI experiments, subjects were instructed to remain still and relaxed in the scanner. Subjects level data were obtained using Phillips scanners and include 33 subjects with eMCI (mean age 72.3, 15M/18F) and 35 healthy controls (mean age 74.6, 14M/21F).

Data were pre-processed using SPM [SPM, 2023], following a standard fMRI preprocessing pipeline. The first 10 volumes were discarded to account for initial scanner and subject noise. Next, a slice timing correction was performed (`spm_slice_timing`) to correct for timing differences between slices within each volume. The images were then realigned using `spm_realign`, which applies a rigid-body transformation to align each volume with the mean functional image. Motion parameters were estimated using least-squares with 2nd degree B-spline interpolation. The estimated motion parameters were subsequently applied to reslice all volumes using 4th degree B-spline interpolation to minimize resampling artifacts. The images were then normalized to the Montreal Neurological Institute (MNI) space with 3mm$\times$3mm$\times$3mm voxels (`spm_normalise`). Nuisance covariates (Friston 24, cerebrospinal fluid, white matter, and global mean) were regressed out. The voxels were then spatially smoothed using a Gaussian kernel (FWHM = 6mm) in `spm_smooth`. A linear trend was removed from each time series using ordinary least squares regression (`spm_detrend`) and a fourth

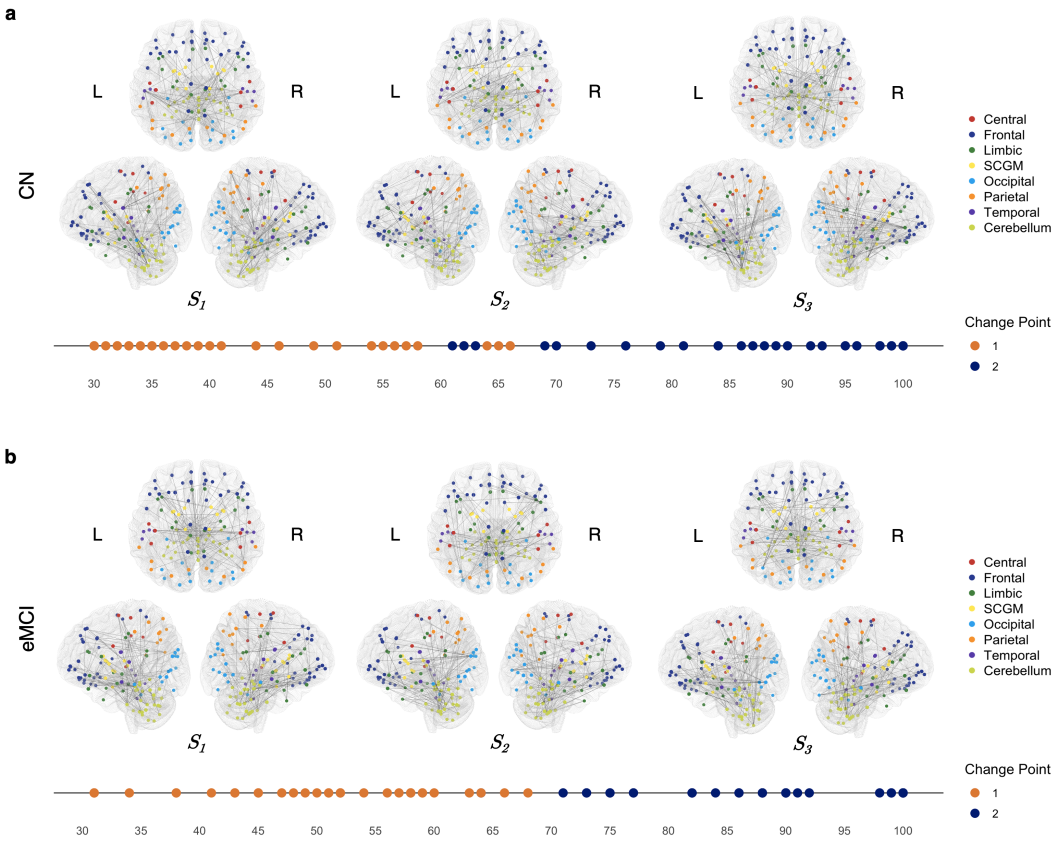


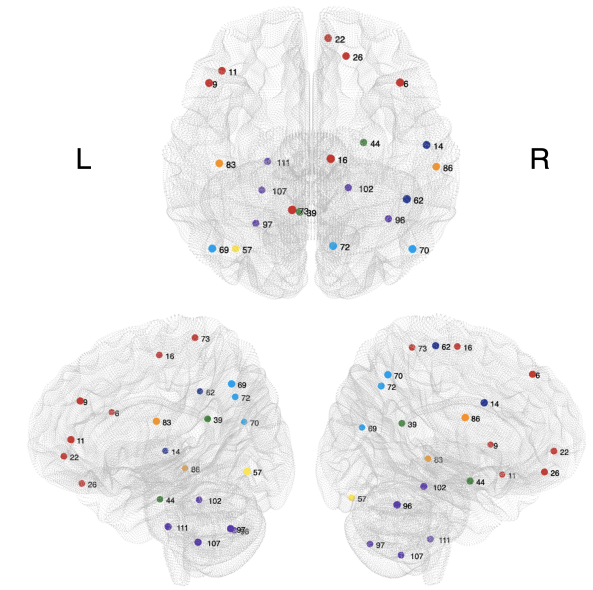
Figure 7: The change point detection results from applying FaBiSearch (taking only the first two change points, FBS_cpDFC2) and corresponding stationary FC states for (a) controls and (b) subjects with eMCI for the ADNI rs-fMRI dataset. For each panel, FC plots are shown for each stationary segment, where $\boldsymbol{S}_1, \boldsymbol{S}_2, \boldsymbol{S}_3$ correspond to the first, second, and third stationary segments. Individual change points are used to segment the time series, and then correlation matrices are averaged across subjects. The top 100 edges as determined by the absolute value of this averaged correlation are shown for each stationary segment. Below the FC plots, orange and blue points indicate the first and second detected change points, respectively, for each subject such that the points are pooled within each group (CN or eMCI).

order Butterworth low-pass filter (0.01–0.08 Hz) was applied to attenuate high-frequency noise and low-frequency drift outside the typical BOLD signal range (`spm_filter`). We used the Automated Anatomical Labeling (AAL2) atlas to subdivide the brain into 120 anatomical regions [Tzourio-Mazoyer et al., 2002]. We chose the AAL2 atlas because of its widespread use in neuroimaging studies, particularly in Alzheimer's disease and MCI research, allowing for comparisons with other works. AAL2 provides whole-brain coverage with a moderate number of parcels, providing a balance between spatial resolution and statistical power. The region of interest (ROI) time series for a given region was defined as the average of the time series of all voxels within that region. Finally, each time series was z-score normalized. The final preprocessed dataset for each subject was a time series of dimension $T = 130$ time points by $p = 120$ ROIs.

C.2 Secondary dataset

In order to check the robustness of our results, we apply our methods to a second study of MCI classification [Mascali et al., 2015], which includes 10 patients with mild cognitive impairment and 10 healthy elderly controls. Participants were told to lie quietly with their eyes closed without falling asleep. A 3T MRI system (Magnetom Allegra, Siemens, Erlangen, Germany) was used to acquire images, with the following properties: TR = 2080 ms, TE = 30 ms, 32 axial slices parallel to the

a



b

Node ID	Folds	Region	Feature	Segment	CN	eMCI
70	68	Parietal	Degree	2	17.029	15.727
107	68	Cerebellum	Betweenness	3	79.675	83.258
6	68	Frontal	Clustering coefficient	3	0.413	0.427
73	68	Frontal	Clustering coefficient	3	0.396	0.439
6	68	Frontal	Local efficiency	3	0.675	0.690
97	68	Cerebellum	Shortest Path	3	3.943	6.030
73	66	Frontal	Local efficiency	3	0.667	0.663
57	42	Occipital	Betweenness	1	86.251	80.899
83	37	Temporal	Betweenness	3	70.976	57.667
111	34	Cerebellum	Shortest Path	3	5.286	10.061
44	29	Limbic	Local efficiency	1	0.515	0.666
9	13	Frontal	Betweenness	1	93.772	60.663
26	10	Frontal	Shortest Path	1	5.229	5.636
9	7	Frontal	Clustering coefficient	1	0.347	0.462
16	6	Frontal	Betweenness	2	52.337	79.090
22	5	Frontal	Local efficiency	1	0.580	0.707
86	4	Temporal	Shortest Path	3	5.000	8.970
73	3	Frontal	Clustering coefficient	1	0.384	0.524
62	3	Central	Local efficiency	3	0.695	0.727
86	2	Temporal	Local efficiency	3	0.676	0.687
62	1	Central	Clustering coefficient	1	0.401	0.508
73	1	Frontal	Local efficiency	1	0.588	0.723
39	1	Limbic	Shortest Path	1	7.000	6.788
14	1	Central	Betweenness	2	84.906	87.841
97	1	Cerebellum	Betweenness	2	84.796	67.681
102	1	Cerebellum	Clustering coefficient	2	0.416	0.488
72	1	Parietal	Betweenness	3	64.736	84.901
62	1	Central	Clustering coefficient	3	0.438	0.493
11	1	Frontal	Local efficiency	3	0.612	0.669
69	1	Parietal	Local efficiency	3	0.685	0.690
96	1	Cerebellum	Shortest Path	3	5.086	6.848

Figure 8: (a) The associated regions of interest (ROIs) of the features selected across all folds by SIS in leave-one-out cross validation for FBS_cpDFC2 in the classification study of CN subjects and subjects with eMCI from the ADNI rs-fMRI dataset. (b) The node ID, the number of LOOCV folds that the feature was chosen, region from the AAL atlas, the graph theoretic feature type, the stationary segment (i.e., 1 = first, 2 = second, 3 = third), and the mean values of the features of the CN and eMCI groups. The features are ordered in descending order based on how often they were selected across the LOOCV folds.

AC-PC plane, matrix = 64 x 64, in plane resolution = 3x3 mm^2, slice thickness = 2.5 mm, 50% skip, flip angle = 70°. Functional images were preprocessed using the Connectivity toolbox [Whitfield-Gabrieli and Nieto-Castanon, 2012]. The initial four volumes were discarded for signal and scanner stabilization, resulting in 216 time points per subject, and images were slice-time corrected and realigned to the first image. More detailed information on the preprocessing steps can be found in Mascali et al. [2015]. Finally, the atlas of Gordon et al. [2016] was used to parcellate the brain into ROIs. To explore the generalizability of our approach while maintaining comparability with the main study (120 ROIs), we selected the Default [Sperling et al., 2010, Buckner et al., 2008], Frontoparietal [Brier et al., 2012], Cinguloparietal [Bai et al., 2009], and Dorsal Attention [Zhou et al., 2008] communities, resulting in a reduced dimensionality of 102 ROIs. This allowed us to test the method on another dataset with slightly different preprocessing and experimental conditions, while keeping the parcellation scale comparable, to assess the robustness of the results.

D Algorithms for time-varying functional connectivity estimation

In this section, we provide a brief overview of the algorithms used to estimate and analyze dynamic functional connectivity, including a standard sliding-window correlation approach and the FaBiSearch change point detection method Ondrus et al. [2025]. For further technical details are available on FaBiSearch, we refer readers to the original publication [Ondrus et al., 2025].

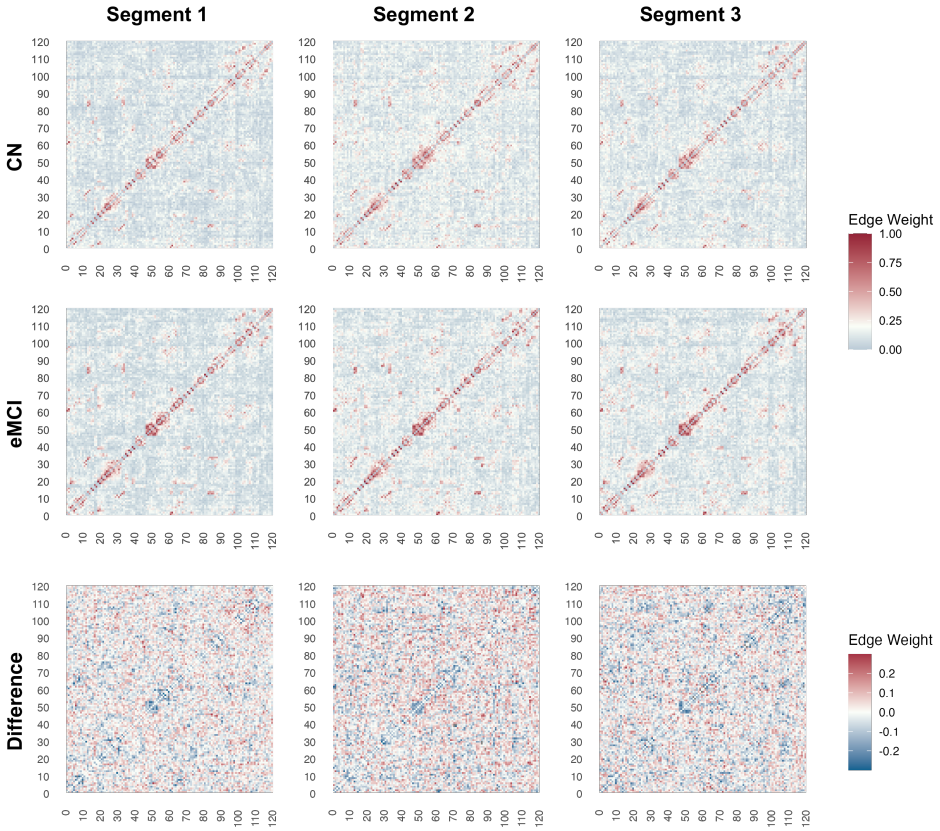


Figure 9: Averaged adjacency matrices across temporal segments (columns), and subject class (rows) for the FaiSearch (cpDFC2) method in the classification study of CN subjects and subjects with eMCI from the ADNI rs-fMRI dataset. Node labels (1 to 120) correspond to the AAL atlas [Tzourio-Mazoyer et al., 2002] labels. The difference between the CN and the eMCI adjacency matrices computed for each segment is shown in the third row.

Algorithm 1: Algorithm for estimating dynamic functional connectivity using sliding windows.

Inputs: fMRI data matrix $\boldsymbol{X}$, window size w, step size s

Initialize the starting point and end points of the window as $t_{\text{start}} = 1$ and $t_{\text{end}} = w$, respectively.

while $t_{\text{start}} + w - 1 \leq T$ **do**

  $t_{\text{end}} \leftarrow t_{\text{start}} + w - 1$

  Estimate FC within the window $\boldsymbol{X}_{t_{\text{start}} : t_{\text{end}}}$

  Advance the window, $t_{\text{start}} \leftarrow t_{\text{start}} + s, \quad t_{\text{end}} \leftarrow t_{\text{start}} + w - 1$

end

Algorithm 2: Change point detection algorithm using FaBiSearch which can be applied recursively to find multiple change points.

Inputs: data matrix $\boldsymbol{X}$, minimum distance δ, number of runs of NMF n_{run}, number of permutation repetitions n_{reps}

Find optimal rank, r, over all of $\boldsymbol{X}$

Evaluate fitments of $\boldsymbol{X}$ to NMF using Kullback-Leibler divergence to navigate over T.

Continue until convergence to a single t which becomes the candidate change point to be evaluated.

Calculate the p-value of the candidate change point to determine whether splitting at this point improves Kullback-Leibler divergence over the null distribution.

E Functional connectivity through graph estimation

We begin by introducing the concept of stationarity, where a stationary segment in the multivariate BOLD time series is defined as one in which the statistical properties are assumed to not change with respect to time [Jones et al., 2012, Handwerker et al., 2012]. The goal of DFC then, is to either model the dynamics of these changing properties, or, to segment the time series to isolate stationary segments. From the DFC approaches outlined in the next section, we obtain a series of stationary segments for each subject, while for SFC, stationary is assumed over the entire experimental time course, and thus one segment is obtained for each subject. For each stationary segment $\mathbf{S}$, we estimate the functional connectivity (FC), or linear dependency, between the ith and jth time series using Pearson's correlation coefficient ρ_{ij}. In the brain fMRI setting, the graph $\mathcal{G} = (V, E)$ is defined such that each vertex $v_i \in V$ represents a region of interest (ROI) or parcellated brain region, and each edge $e_{ij} \in E$ is weighted by the corresponding correlation ρ_{ij} between ROI time series i and j. Because we are primarily interested in strong functional connections, we apply an absolute correlation threshold of 0.5, consistent with the range (0.1–0.8) commonly used in the literature [Adamovich et al., 2022]. Thus, an edge e_{ij} remains in $\mathcal{G}$ if $|\rho_{ij}| > 0.5$. A schematic of the SFC estimation procedure is shown in Figure 1(b). The resulting adjacency matrix encodes the network structure for the segment, with retained edge weights reflecting the strength of functional coupling between brain regions as measured by correlation. More formally, let $\tau = 0.5$. The edge set is

$$E = \big\{\{i, j\} : i < j,\ |\rho_{ij}| > \tau\big\},$$

and the weighted adjacency is $A_{ij} = \rho_{ij}$ if $\{i, j\} \in E$ and $A_{ij} = 0$ otherwise (with $A_{ii} = 0$).

F Estimating DFC

To estimate DFC, we assume that we have no prior knowledge of the distribution of $\boldsymbol{X}$, and that there may be an unknown number of distributional shifts, with the number and locations in $\{1, \ldots, T\}$ and the rate of change between them is assumed unknown. We do however assume that there exist segments in $\boldsymbol{X}$ which *are* stationary. We consider two approaches, sliding windows (swDFC) and change points (cpDFC), for estimating time-varying connectivity in rs-fMRI. swDFC is a naive approach in which no data information is used to determine the temporal structure. Here, a window of a particular length, w, is used to subselect the set of time indices in $\{1, \ldots, T\}$. As its name suggests, the window is then slid over a predetermined length, s, to define the next window. Consequently, the sliding window captures dynamic information by subsampling the entirety of the distribution through a predetermined and overlapping set of time-dependent steps, where within each of these windows, FC is estimated as described in Section E. We describe the sliding-window method in Algorithm 1 (in the Appendix) and show a schematic in Figure 1(c).

The choices for w and s are crucial, as they determine the granularity and the amount of overlap between snapshots that this technique captures. However, the values for these parameters are context dependent and it is not possible to derive them directly from $\boldsymbol{X}$. As a consequence of this, we vary the combinations of w and s in our experiments and test the classification performance.

We implement cpDFC using FaBiSearch, a change point detection technique in the network structure between (high-dimensional) multivariate time series [Ondrus et al., 2025]. More formally, we consider the multiple change point detection problem in a multivariate time series data $\boldsymbol{X}$. We seek to find the time points where the network structure of $\boldsymbol{X}$ changes. FaBiSearch utilizes non-negative matrix factorization (NMF: Lee and Seung, 1999) to identify multiple change points in high-dimensional time series data. In particular, change points are identified in a sequential manner through successive splitting of the time series. No limit is imposed on the number of change points; instead, detection proceeds until further splitting cannot be performed. Candidate change points are then evaluated through a permutation test procedure. The method requires a series of hyperparameters; $\boldsymbol{X}$, α, δ, n_{run}, n_{reps}, r which refer to the input multivariate time series data, significance for the permutation test, minimum distance between change points, maximum number of runs of the NMF algoirthm, and the number of permutation in the permutation test. The rank of NMF to use in the procedure, r, can be determined from the data by an iterative permutation procedure. Algorithm 2 (in the Appendix) summarizes FaBiSearch, and we utilize a loss based on Kullback-Leibler divergence to assess the fit of the model. For more details on FaBiSearch, see Ondrus et al. [2025].

In contrast to the sliding window method, which can be highly sensitive to the precise choice of parameters such as window length and step size, Change point detection does not require parameter values to be so finely tuned for optimal performance. Instead, it only requires sufficient settings, meaning enough data samples, permutation iterations, and related hyperparameters, to reliably detect change points, without the need to identify a single "best" configuration. Ondrus and Cribben [2024] show through a sensitivity analysis on simulated data that the accuracy of change point detection using FaBiSearch plateaus beyond sufficient values of the input hyperparameters. In their simulations, Ondrus and Cribben [2024] found that performance plateaued once $\delta \geq 30$, $nrun \geq 100$, $nreps \geq 100$, denoting the minimum distance between change points, the number of NMF runs for convergence, and the number of permutations for the significance test, respectively. Increasing these values beyond these thresholds produced only marginal improvements in detection accuracy.

For each subject, we first estimate the change points using FaBiSearch and then order the change points $\hat{q}$ by their respective p-value from smallest to largest. After defining the set of change points, $\hat{q}$, we partition $\boldsymbol{X}$ into stationary time segments between the change points. In the classification study, we used $k = 1$ and $k = 2$ change points to define the stationary segments. Finally, for each of the stationary segments, we estimate FC as described in Section E.

We also estimate cpDFC using two other change point detection methods, specifically Network Change Point Detection (NCPD: Cribben and Yu, 2017) and Covariance Change Points through Random Matrix Theory (CRMT: Ryan and Killick, 2023). For NCPD and CRMT, we used similar hyperparameters to FaBiSearch, that is, a similar minimum distance between the change points and the optimal rank. All other hyperaparameters for these methods were set to their default values. For CRMT, we further pre-processed ROI time series by performing a truncated SVD with the same optimal rank as used in FaBiSearch to satisfy the theoretical condition that $p \leq n$ for the estimator to be well-behaved. A schematic of change point detection is shown in Figure 1(d).

G Graph Theoretic Features

Degree

The degree of a node can be calculated from the following definition:

$$d_i = \sum_{j \in V} a_{ij} \ ,$$

where $d_i \in \mathbb{N}_0$ is the degree of the node i, V is the set of all nodes, and a_{ij} is the intersection of the nodes i and j in the adjacency matrix.

Clustering coefficient

From Wasserman and Faust [1994], it is given by:

$$C_i = \frac{2e_i}{d_i(d_i - 1)} \ ,$$

where $C_i \in [0, 1]$ is the clustering coefficient for node i, d_i is the degree of node i, and e_i is the number of edges between node i and neighbors d_i.

Shortest path

We use the notation $\ell_{ij} \in \mathbb{N}_0$ as the fewest number of edges that connect nodes i and j together to define the shortest path. The shortest path can be calculated using different algorithms, although we use breadth-first search (BFS: Cormen et al., 2022) in our implementation.

Degree assortativity

Newman [2002] define degree assortativity as

$$r_{jk} = \frac{m^{-1}\sum_i j_i k_i - \left[m^{-2}\sum_i \frac{1}{2}(j_i + k_i)\right]^2}{m^{-1}\sum_i \frac{1}{2}(j_i^2 + k_i^2) - \left[m^{-2}\sum_i \frac{1}{2}(j_i + k_i)\right]^2}$$

where $r \in [-1, 1]$ is the degree assortativity of the graph, m is the total number of edges, and j_i and k_i are the degree of the nodes j and k that are connected through i.

Local efficiency

The definition of local efficiency from Latora and Marchiori [2001] is

$$E_i = \frac{1}{d_i(d_i - 1)} \sum_{j,k \in G_i, j \neq k} \frac{1}{\ell_{jk}} ,$$

where $E_i \in [0, 1]$ is the local efficiency measure of node i, d_i is the degree of node i, and ℓ_{jk} is the shortest distance between nodes j and k in the sub-graph of $\mathcal{G}_i$.

Betweenness centrality

The definition of betweenness centrality [Freeman, 1977] follows:

$$B_i = \sum_{j \neq i \neq k} \frac{\sigma_{jk}(i)}{\sigma_{jk}} ,$$

where $B_i \in [0, 1]$ is the betweenness centrality of node i, σ_{jk} is the total number of shortest paths between nodes j and k, and $\sigma_{jk}(i)$ is the total number of shortest paths between j and k that pass through i.

H Evaluation metrics

We evaluated the performance of our models from the classification study using the following four metrics:

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}$$

$$\text{Sensitivity} = \frac{TP}{TP + FN}$$

$$\text{Specificity} = \frac{TN}{TN + FP}$$

$$F_1 = 2 \times \frac{\text{Precision} \times \text{Recall}}{\text{Precision} + \text{Recall}}$$

where $\text{Precision} = \frac{TP}{TP + FP}$, $\text{Recall} = \frac{TP}{TP + FN}$ and ,

TP denotes True Positives; The number of correctly labeled eMCI.

TN denotes True Negatives; The number of correctly labeled control.

FP denotes False Positives; The number of control incorrectly labeled as eMCI.

FN denotes False Negatives; The number of eMCI incorrectly labeled control.

I Data, code, and computational resources statement

Due to the sensitive nature of the data used in this study, as well as the terms of use for both sources, we are unable to directly share the data used. The ADNI and Mascali et al. [2015] datasets used were derived from the following public domains `http://adni.loni.usc.edu/` and `https://dataverse.harvard.edu/dataverse/restAD`, respectively. All `R` code implementing experiments is available on Anonymous GitHub. All experiments were performed using 48 core machines with 2 Intel Platinum 8260 Cascade Lake at 2.4Ghz and 187GB of memory.

J Potential societal impacts

Our study provides evidence of more accurate and robust estimates of early neurodegeneration, which can accelerate fundamental neuroscience research, improve biomarkers for neurological and psychiatric disorders, and ultimately inform better diagnostics and therapies. However, there are potential negative impacts. For one, there is a risk of misinterpretation of models. Treating the edges of a correlational network as causal may prompt unsafe interventions. Another concern is privacy. High-resolution connectomes can, in principle, carry individual-specific signatures. Sharing or pooling data without adequate safeguards risks misuse of participants' brain data. There are also risks in using this method in unintended ways, such as outside clinical or research contexts (e.g., surveillance of cognitive states). Lastly, there are considerations regarding fairness. If the method is applied to heterogeneous populations without proper care, estimates can systematically misrepresent under-studied groups (e.g., age, ethnicity), leading to biased conclusions.

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