Statistical Methods for Dynamic Connectivity Analysis in Resting State fMRI

Mark Fiecas, in collaboration with

Rebecca Killick, Ellery Island, Meng Xu, and Kathryn Cullen, among others

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1. What is dynamic connectivity?

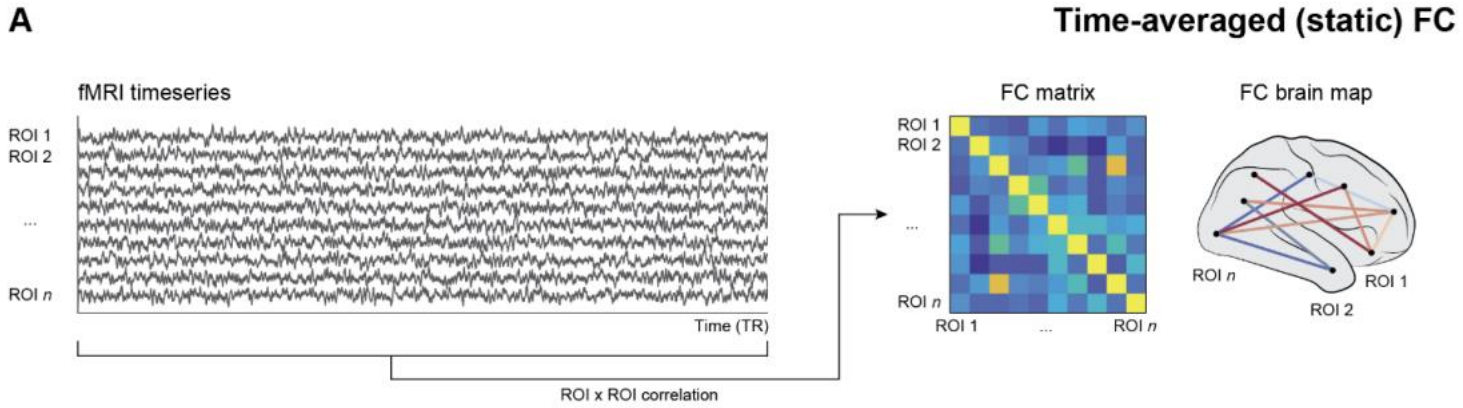
2. How do we use hidden Markov models to model dynamic connectivity in fMRI time series data?

3. How do we use changepoint analysis to model dynamic connectivity in fMRI time series data?

4. What does a dynamic connectivity analysis look like?

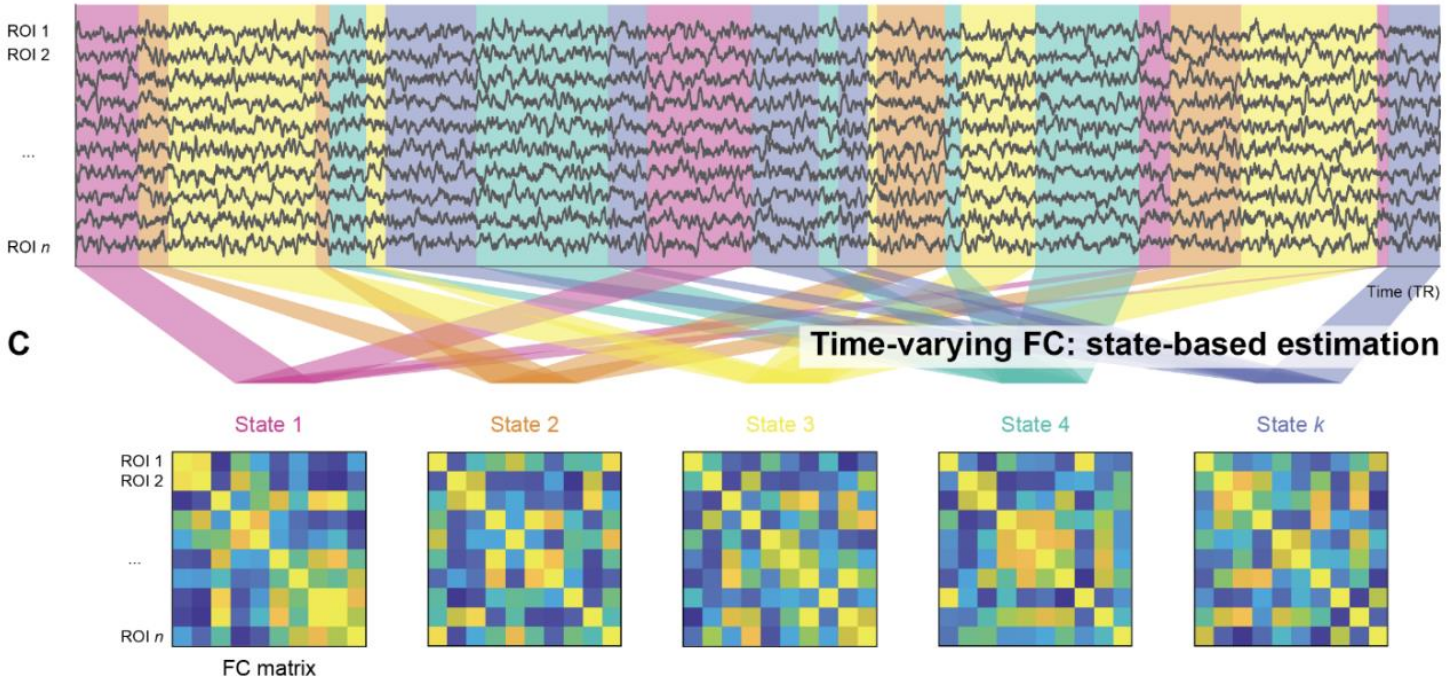
What is dynamic connectivity?

Functional connectivity in fMRI is captured by the correlation matrix of the time series data.



Ahrends and Vidaurre, 2023

The correlation matrix might exhibit “temporal dynamics”.



Ahrends and Vidaurre, 2023

There remains a number of open questions and areas for development in dynamic connectivity analyses.

Questions and controversies in the study of time-varying functional connectivity in resting fMRI

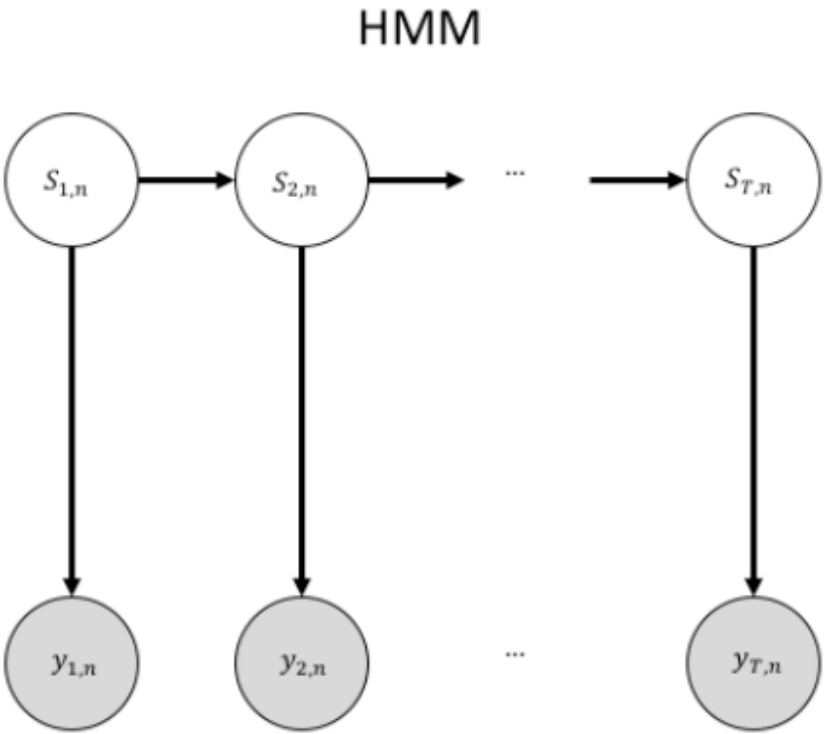
Daniel J. Lurie,[*†] Daniel Kessler,[†] Danielle S. Bassett, Richard F. Betzel, Michael Breakspear, Shella Kheilholz, Aaron Kucyi, Raphaël Liégeois, Martin A. Lindquist, Anthony Randal McIntosh, Russell A. Poldrack, James M. Shine, William Hedley Thompson, Natalia Z. Bielczyk, Linda Douw, Dominik Kraft, Robyn L. Miller, Muthuraman Muthuraman, Lorenzo Pasquini, Adeel Razi, Diego Vidaurre, Hua Xie, and Vince D. Calhoun[*†]

NETWORK NEURO SCIENCE

How do we use hidden Markov models to model dynamic connectivity in fMRI time series data?

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A hidden Markov model assumes that a hidden state sequence drives the properties of the observed data.

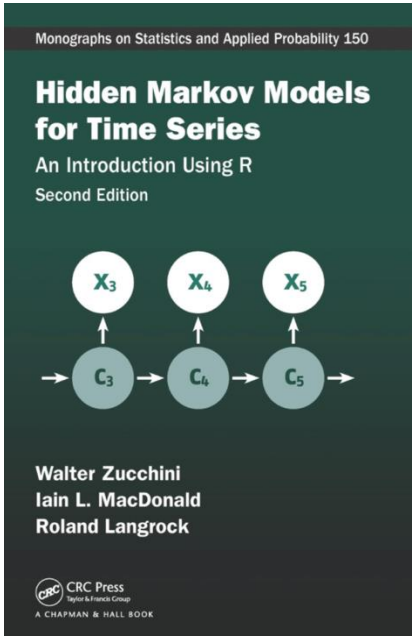


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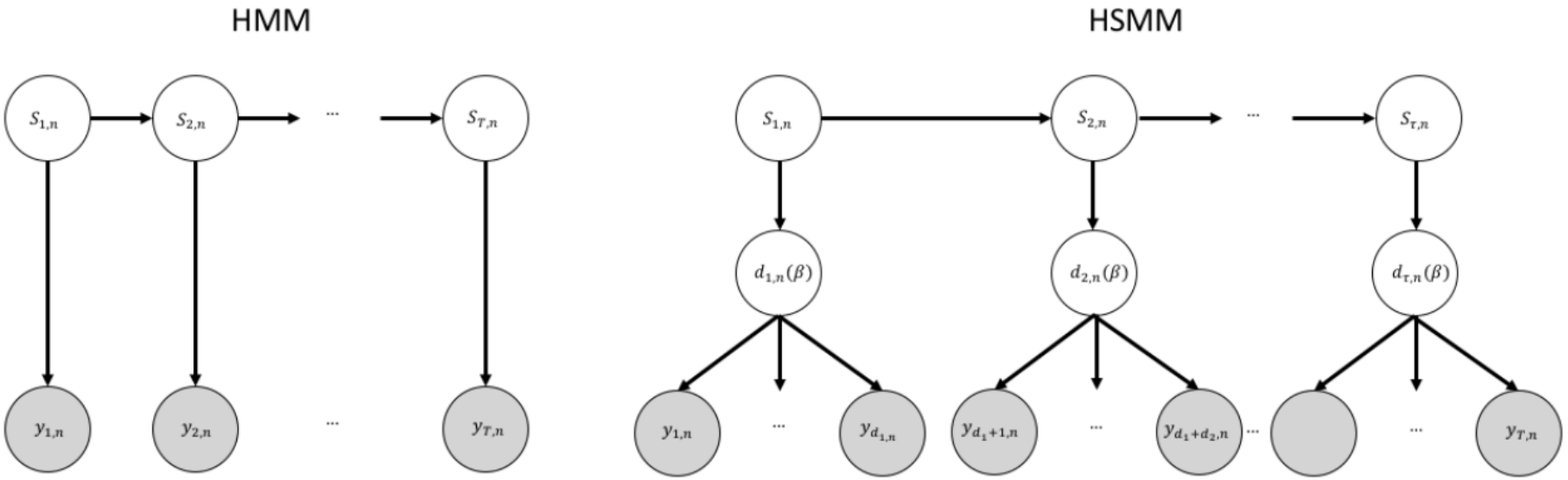
Parameters:

1) Transition probability matrix
2) Parameters of the “emission distribution”

There have been a number of theory and methods developments for hidden Markov models, and software is readily available.

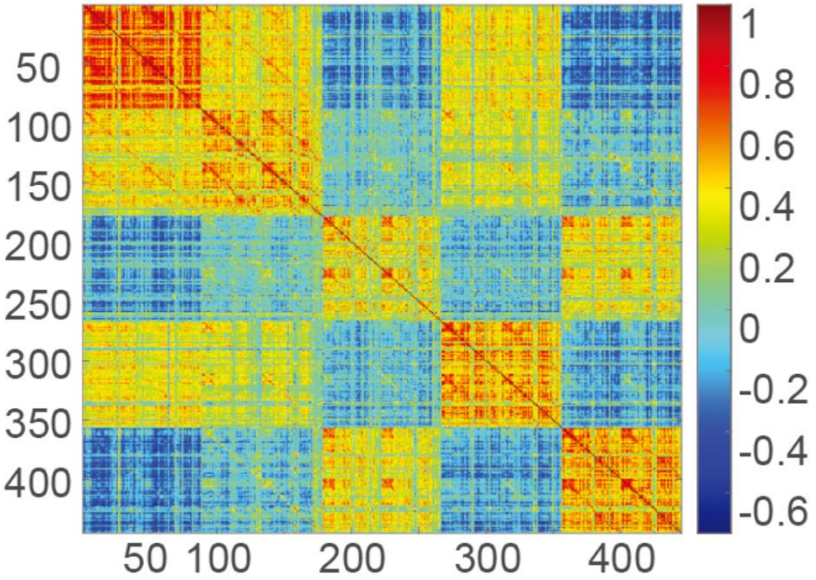


Hidden *semi*-Markov models have an explicit model of the *duration distribution* for the hidden states.



How do we use changepoint analysis to model dynamic connectivity in fMRI time series data?

The correlation matrix of fMRI time series data usually contains structure.



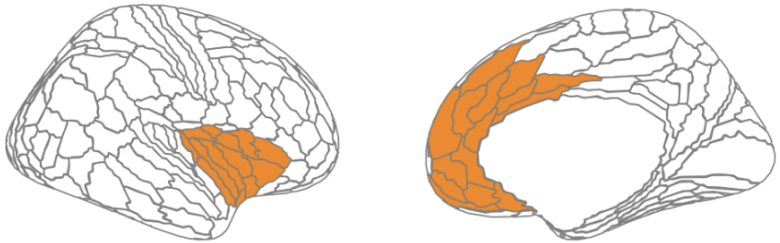
Yang et al, 2023

We model the time series data using a mixed model with variance components that capture the structure in the data.

$$y_{i,j} = \mu + \mu_i + \epsilon_{i,j}$$

Region *i*, parcel *j* within region *i*

Frontolimbic Network



We assumed a block structure for the correlation matrix.

$$(\boldsymbol{\Sigma}_{kk'}) := \begin{pmatrix} \boldsymbol{\Sigma}_{11} & \boldsymbol{\Sigma}_{12} & \dots & \boldsymbol{\Sigma}_{1K} \\ \boldsymbol{\Sigma}_{21} & \boldsymbol{\Sigma}_{22} & \dots & \boldsymbol{\Sigma}_{2K} \\ \vdots & \vdots & \ddots & \vdots \\ \boldsymbol{\Sigma}_{K1} & \boldsymbol{\Sigma}_{K2} & \dots & \boldsymbol{\Sigma}_{KK} \end{pmatrix}$$

$$= \Sigma_\epsilon + \Sigma_\mu \circ \mathbf{J}(\mathbf{k})$$

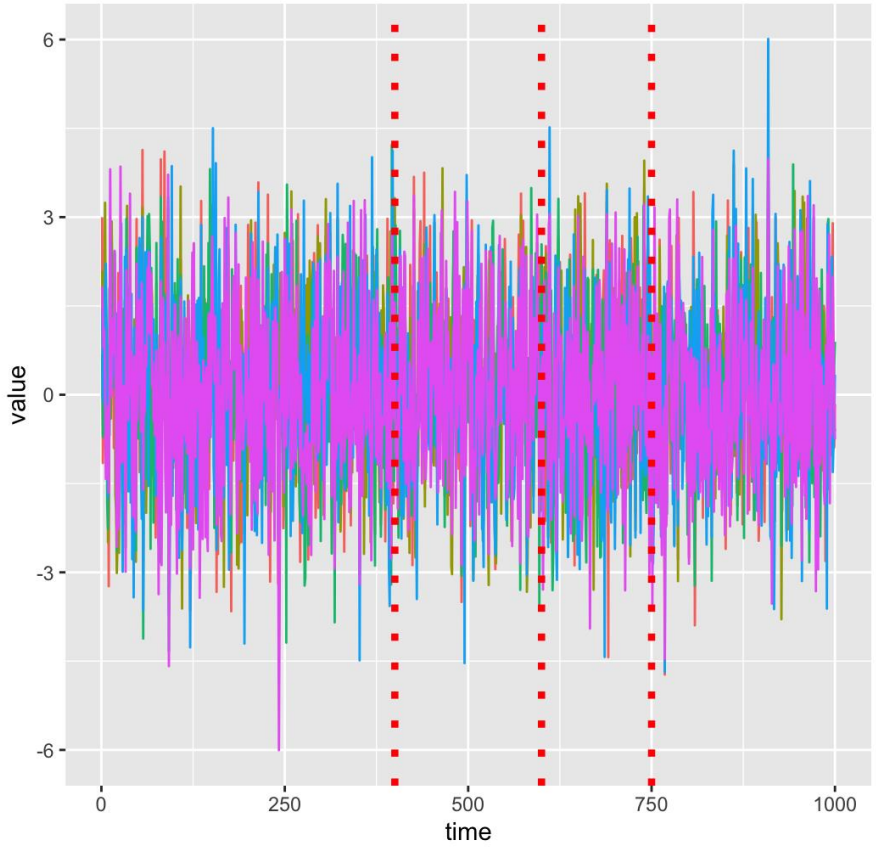
We used PELT (**P**runed **E**xact **L**inear **T**ime), a dynamic program algorithm for estimating the number and location of changepoints.

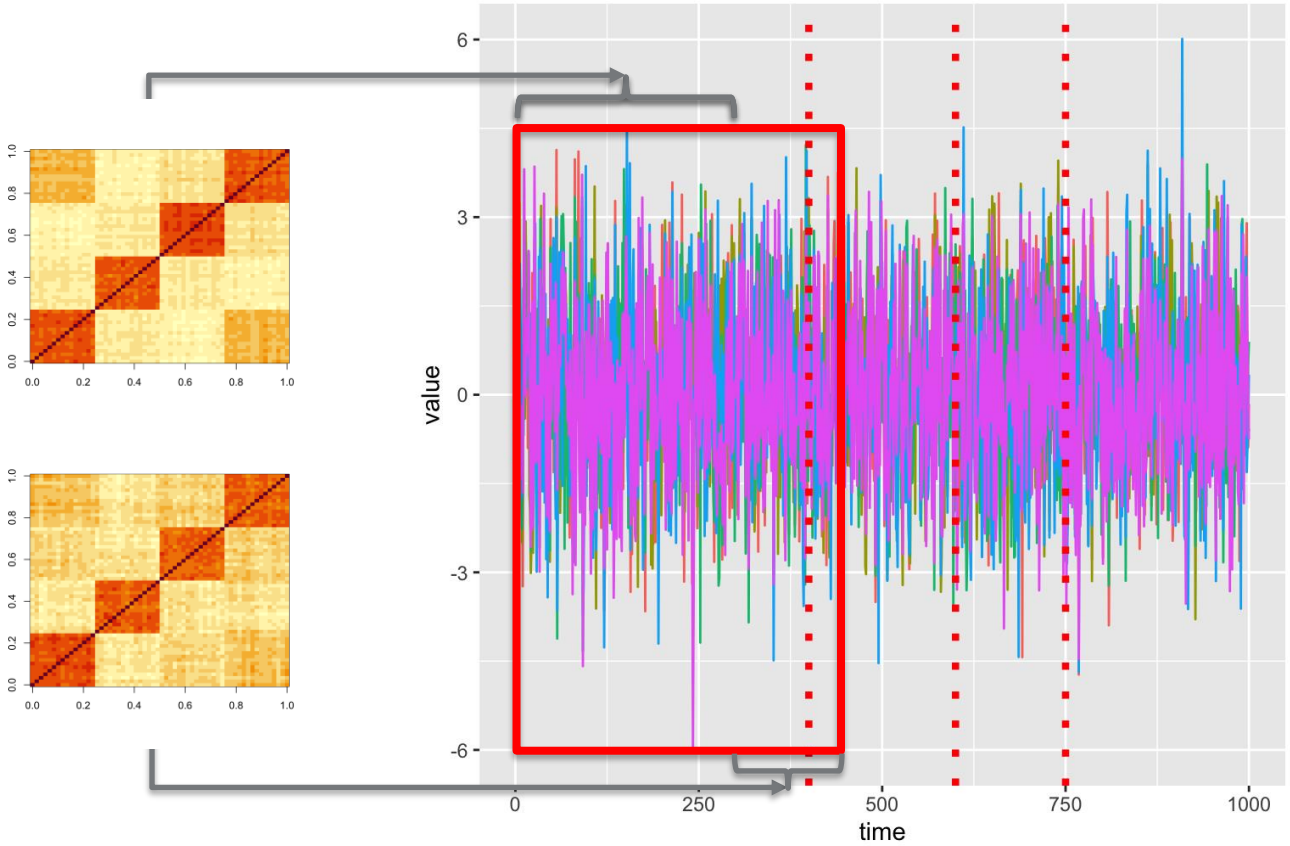
Briefly, the goal is to optimize

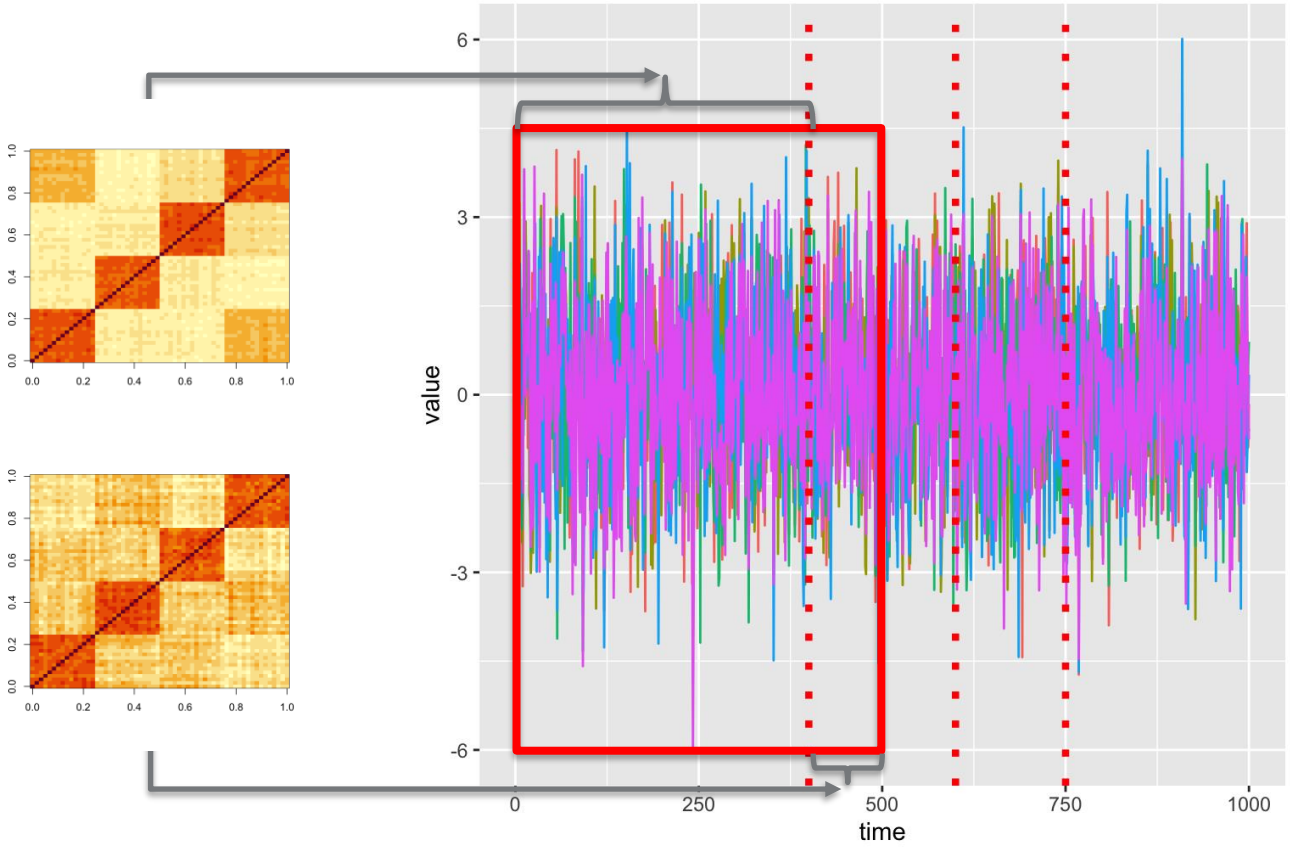
$$\sum_{m=0}^{M} \sum_{s=\tau_m+1}^{\tau_{m+1}} Cost\left(\boldsymbol{y}_s \middle| \hat{\theta}_m\right) + CMlog(n)$$

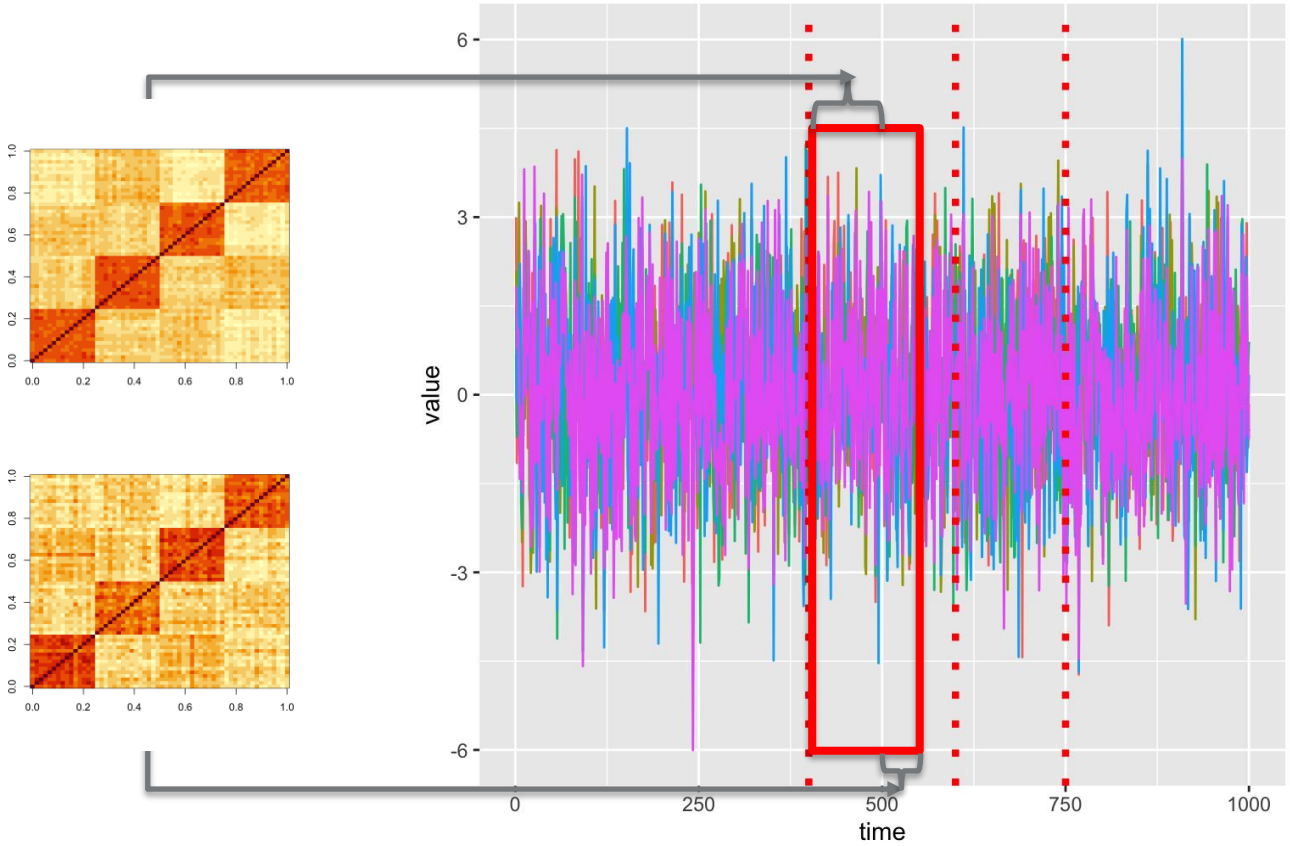
Optimal Detection of Changepoints With a Linear Computational Cost

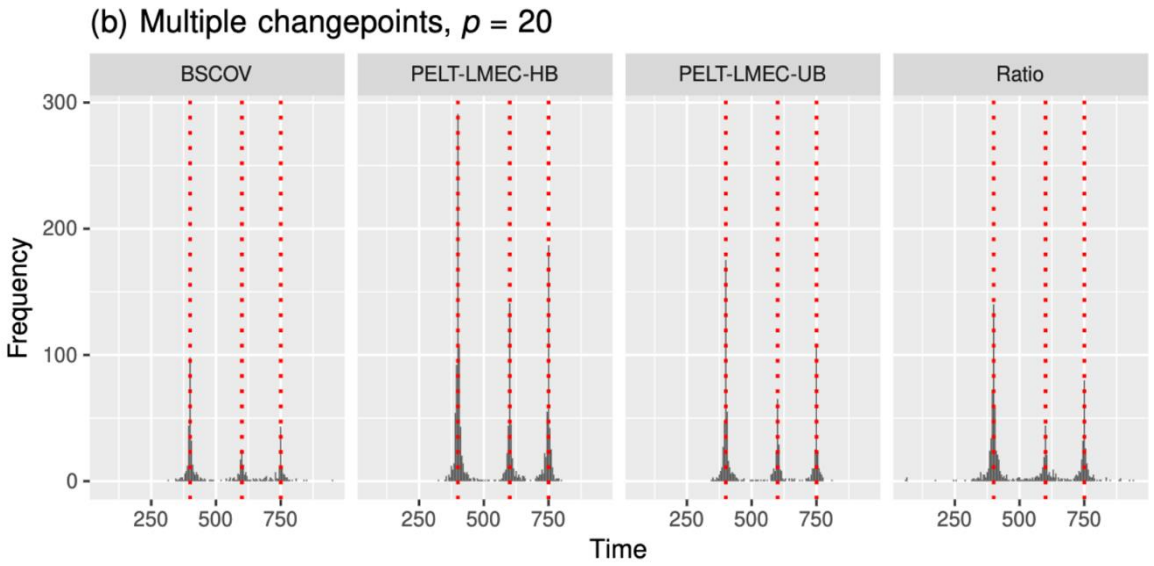
R. KILLICK, P. FEARNHEAD, and I. A. ECKLEY


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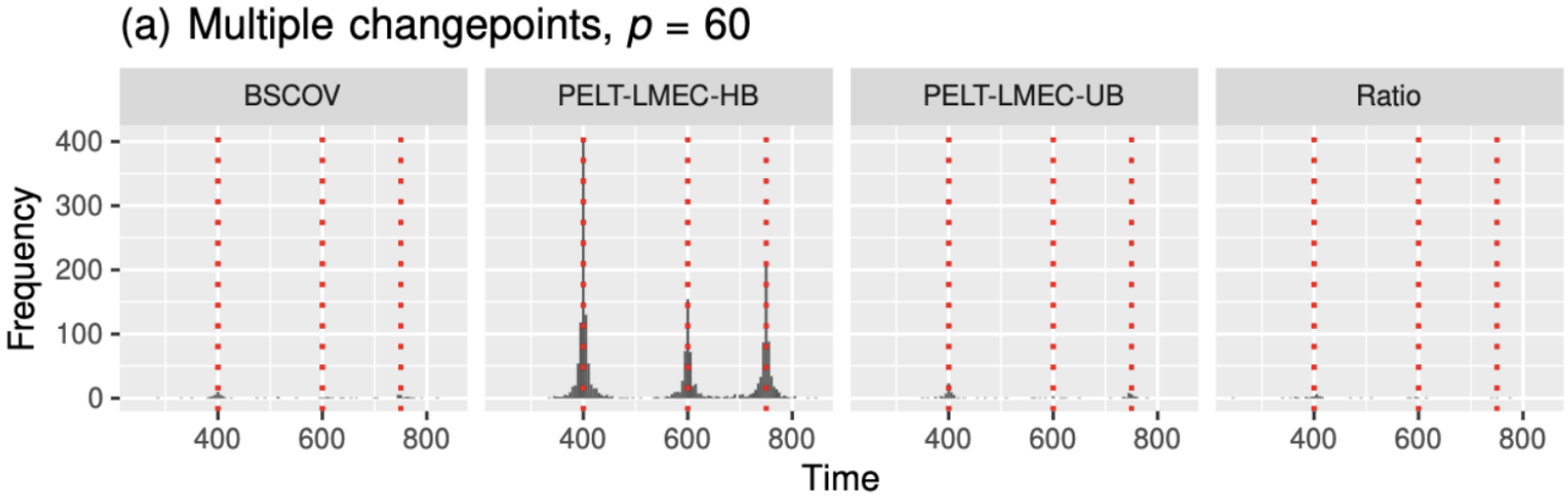

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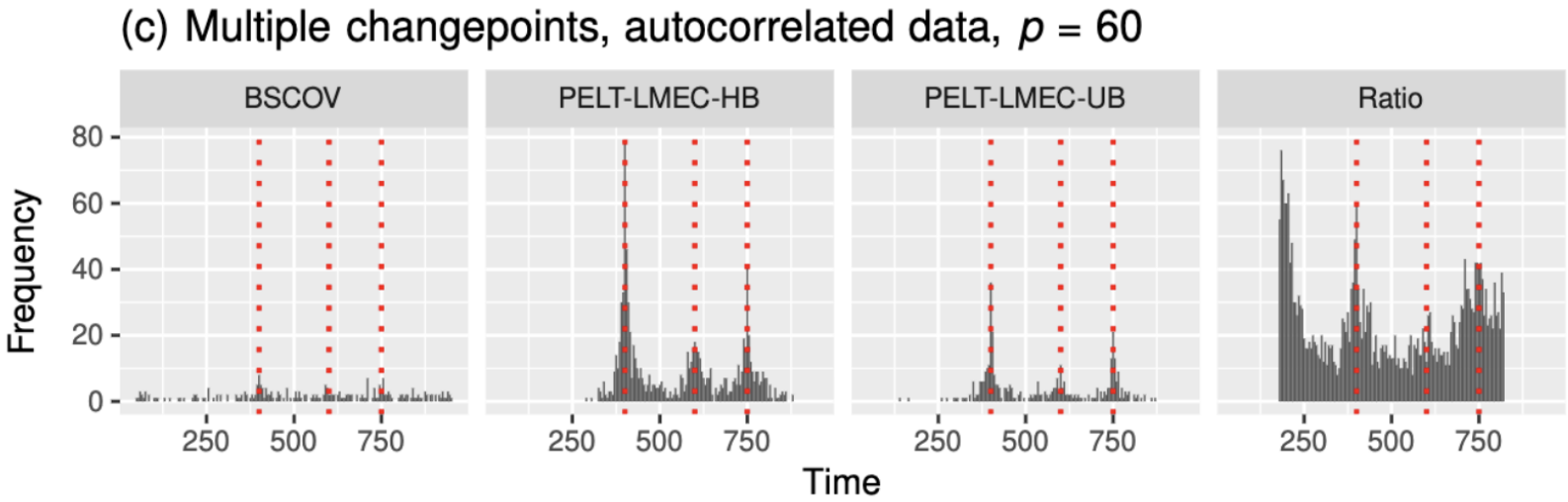

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Fiecas et al, 2026



Fiecas et al, 2026



Fiecas et al, 2026

Summary of the method:

1. Mixed model framework with structured covariance matrices

2. Method-of-moments for estimation of the covariance matrices

3. PELT for changepoint estimation

What does a dynamic connectivity analysis using fMRI data look like in practice?

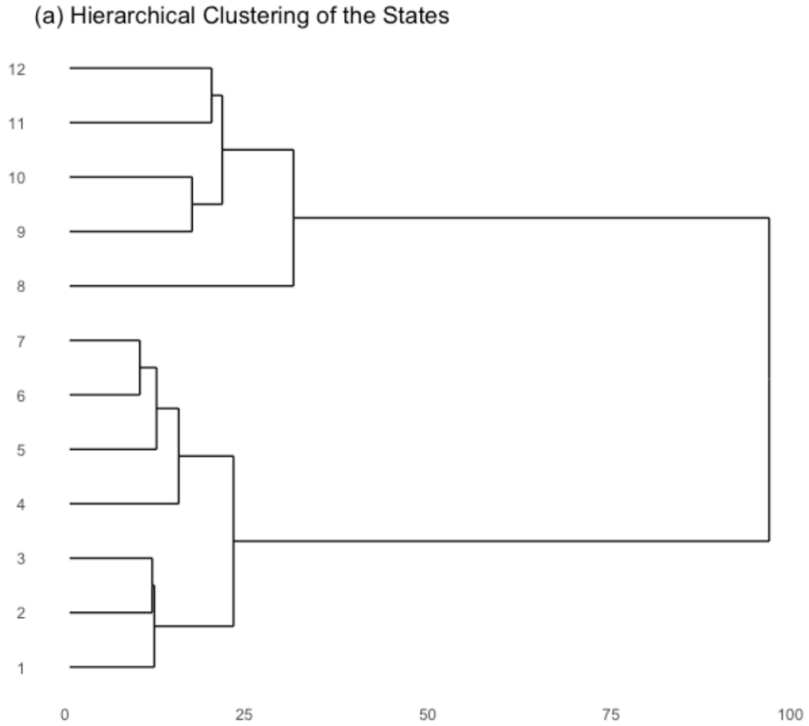
Brain Imaging Development of Girls' Emotion and Self (BRIDGES) for studying non-suicidal self-injury (NSSI)

- Ongoing longitudinal study. We focus on the baseline data.
- N=126, 12-16 years of age
- Classified to 4 categories: 48 with no or mild NSSI, 78 with moderate or severe NSSI
- Spatial ICAs from the GIFT toolbox used to obtain 41 regions of interest
- # time points = 902

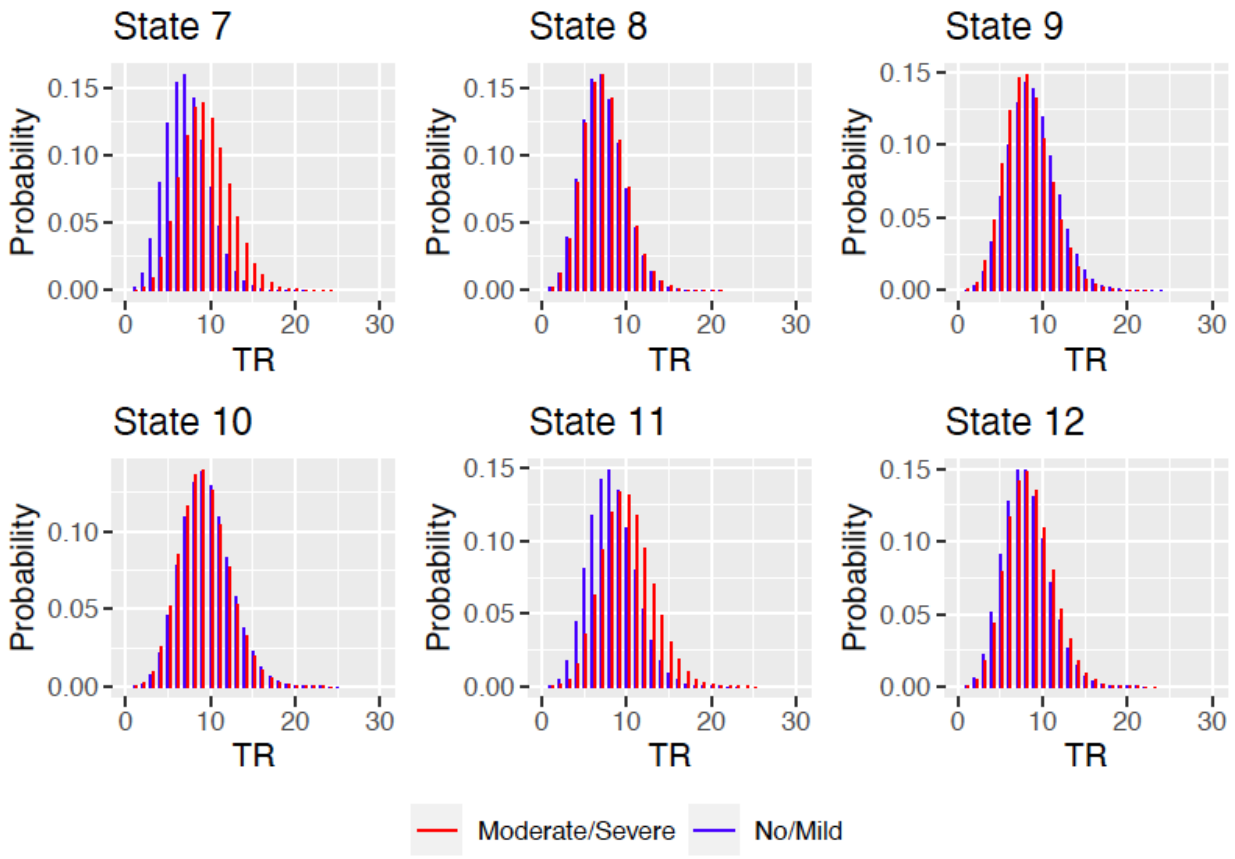
Model settings

- 12-state approximate HMM and HSMM model
- Shifted Poisson distribution, rate parameter a function of NSSI severity
- Permutation test for statistical inference

Posthoc clustering of the states suggested the existence of “meta-states”, in agreement with existing findings.

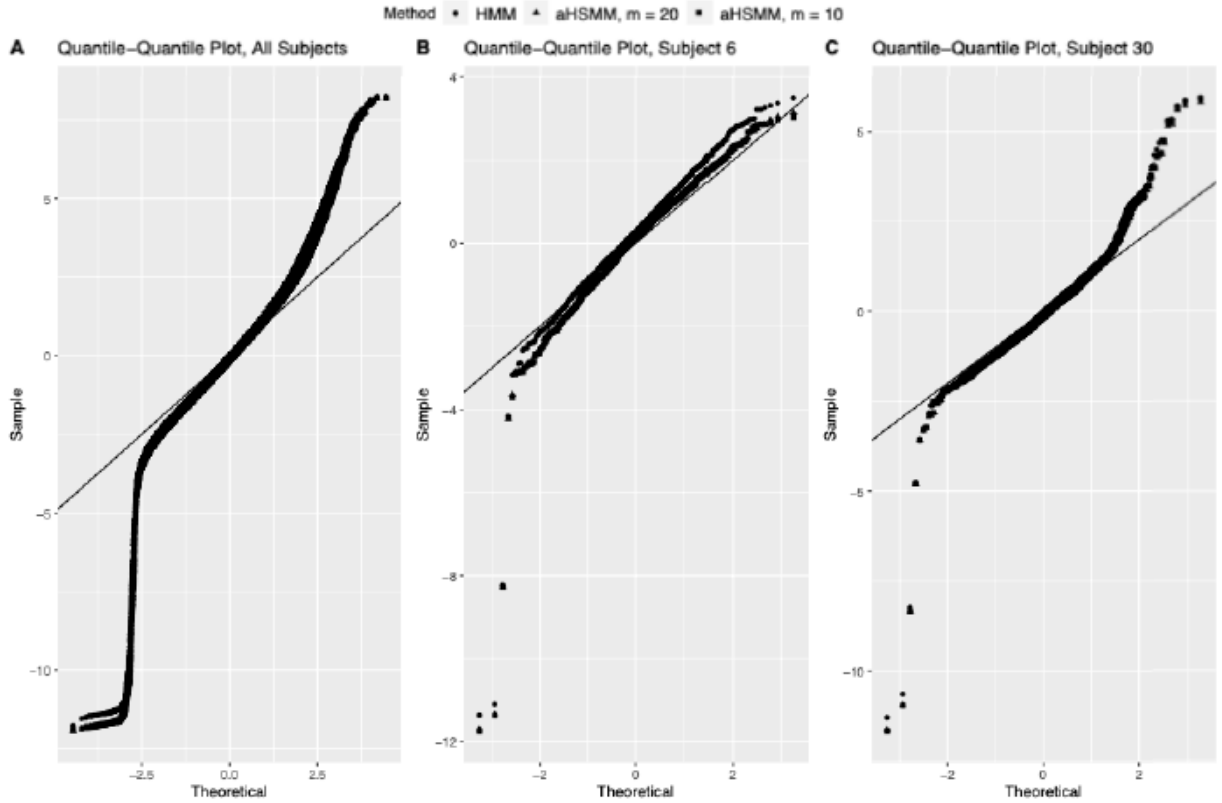


Fiecas et al, 2023



Fiecas et al, 2023

The pseudo-residuals suggest poor model fit overall.



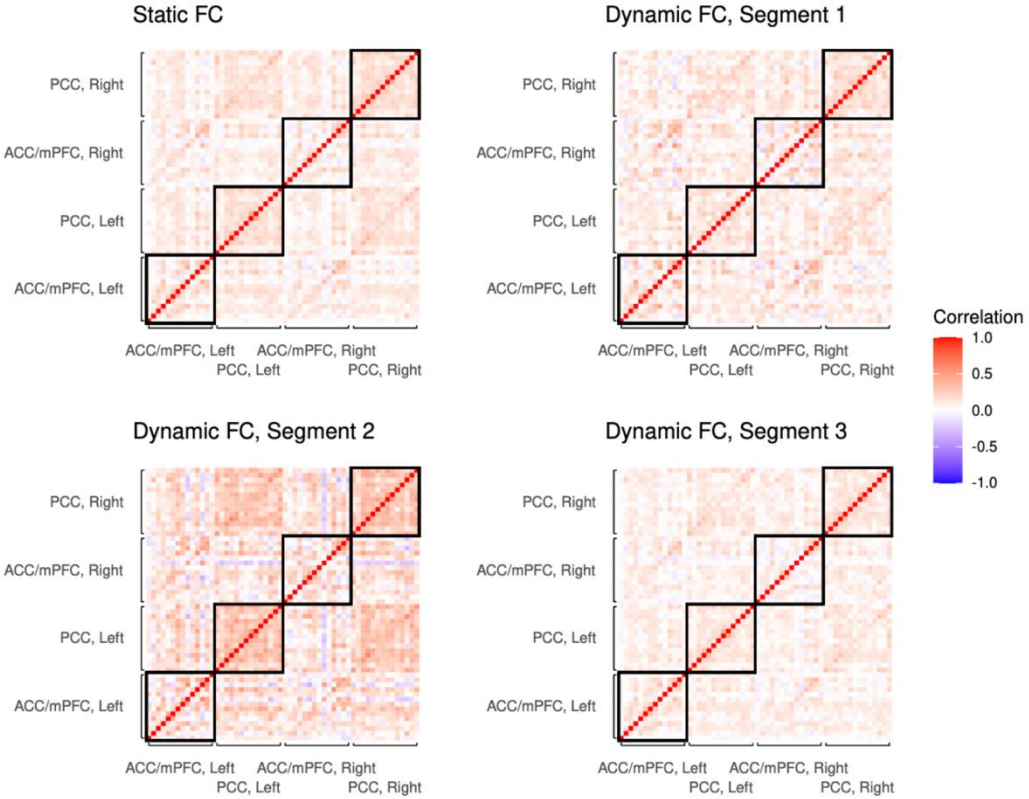
Fiecas et al, 2023

Changepoint Analysis: Model settings

- Analysis restricted to the Glasser parcels within the Default Mode Network (56 dimensions total)

- Time series were prewhitened prior to analysis

Correlation matrix between segments for one person



Posthoc analysis:

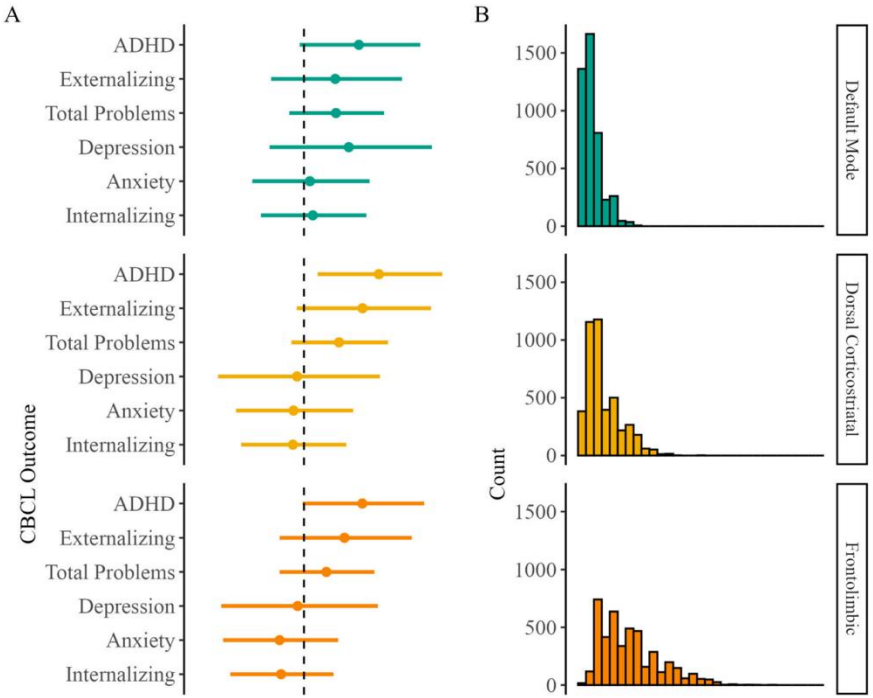
- Number of changepoints was extracted per person and used as an outcome in a Poisson regression model.

- Poisson regression showed that those who presented NSSI symptoms **had more changepoints** relative to those with no NSSI.

Adolescent Brain Cognitive Development (ABCD) Study

- Ongoing longitudinal study. We focus on the baseline resting-state fMRI data.
- Data restricted to the low-motion youths (FD < 0.3mm)
- Data prewhitened to remove autocorrelation
- N=4424, 9-10 years of age
- Varying number of runs per youth

Associations between the number of changepoints and various measures of psychopathology were weak.



Island et al, 2026

Final thoughts

HMMs (and HSMMs)

- There is a broad literature for theories and methods related to HMMs.
- A ”vanilla” HMM model does not characterize the data very well. It is not clear how this affects downstream inference.
- The selection of the number of states and subsequent interpretation are not clear.

Changepoints

- There is a broad literature for theories and methods for changepoint analysis for univariate data; the literature is very sparse for multivariate data.

- Leveraging the block structure in the covariance matrix helps make the dimensionality of the problem more manageable.

- Shifts are “global” and “abrupt”.

Thank you!