Cognitive correlates of BOLD Resting-State Dynamic Functional Connectivity

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National Institute of Mental Health, Bethesda, MD

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Section on Functional Imaging Methods

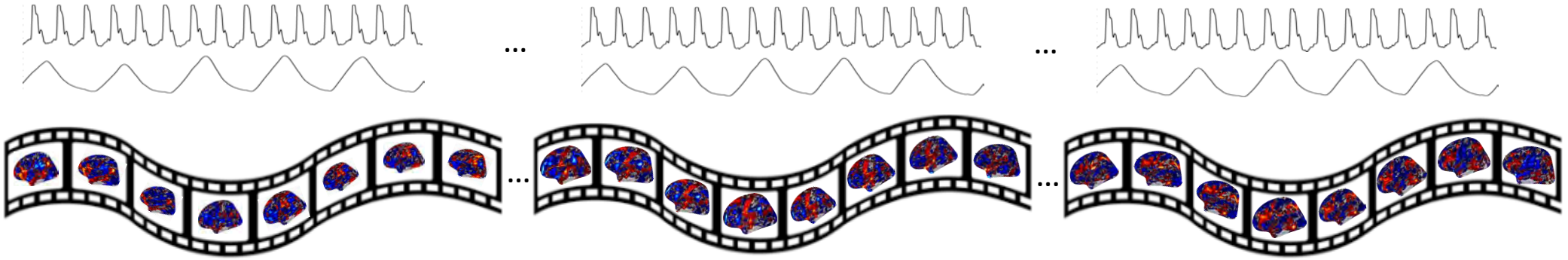
NIH National Institute of Mental Health

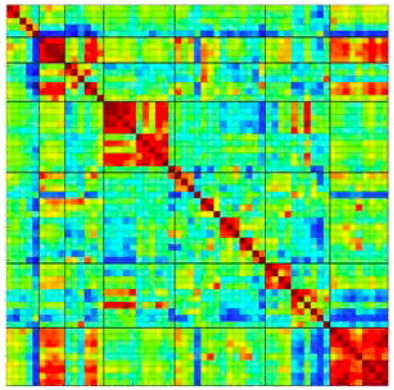
Mental Life

Physiology

Brain

MISSING MISSING MISSING





Mean Effect – Static Functional Connectivity

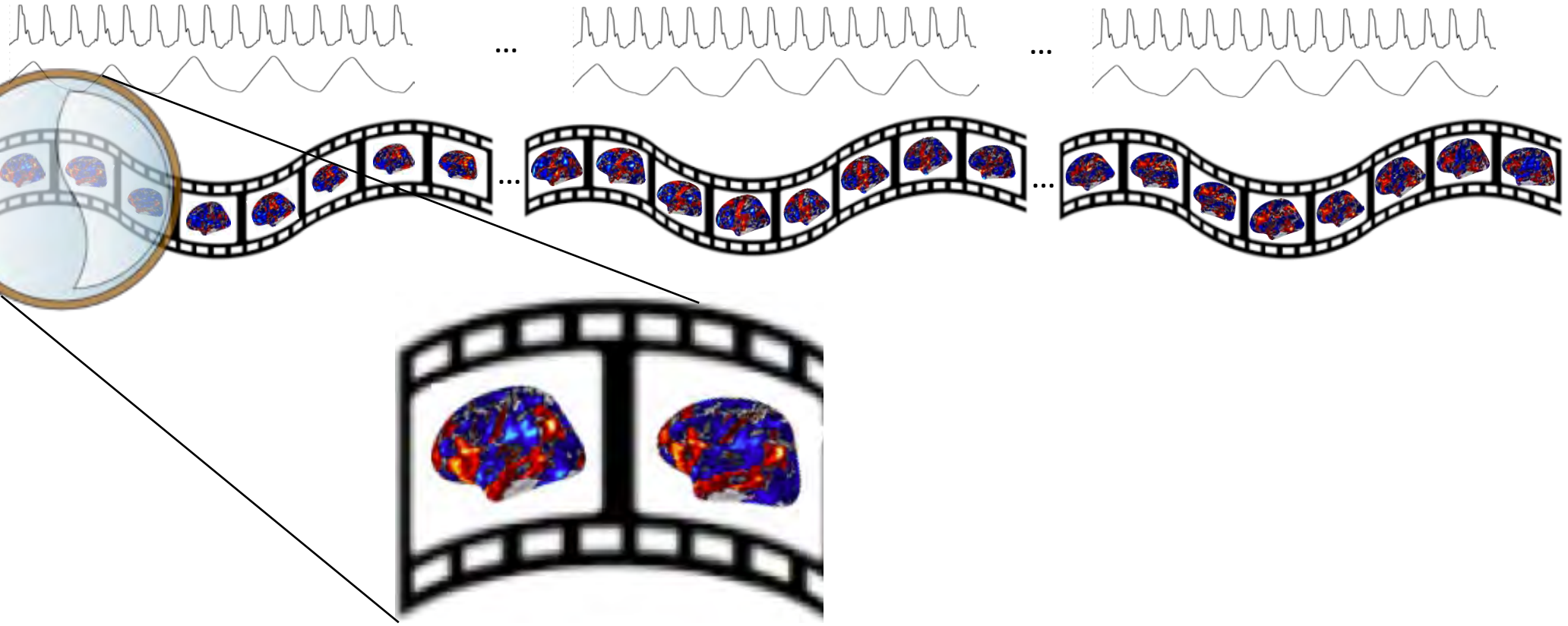
Introduction: Resting State

Mental Life

Physiology

Brain

MISSING MISSING MISSING



Introduction: Resting State

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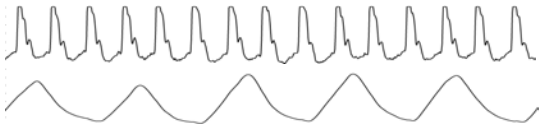
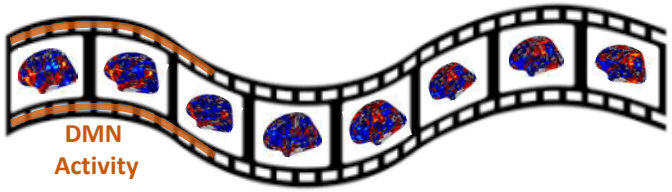
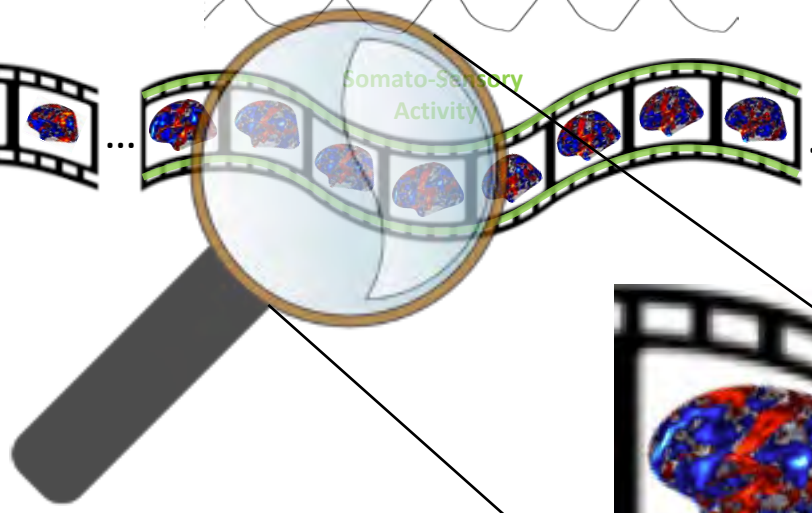
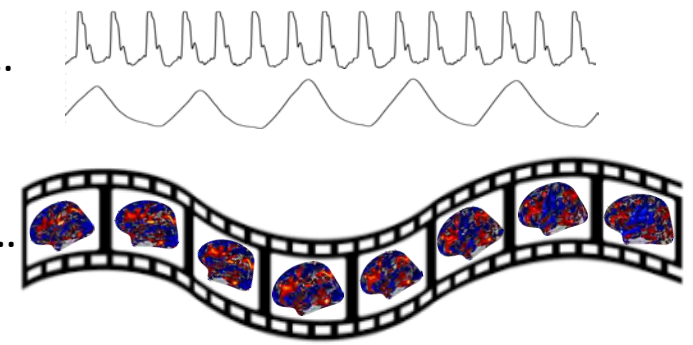


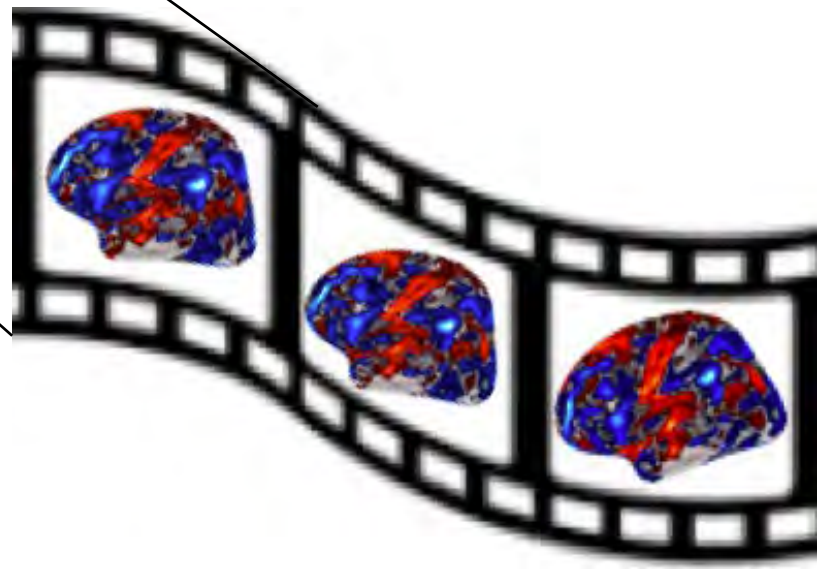


DMN Activity



Somato-Sensory Activity





Mental Life

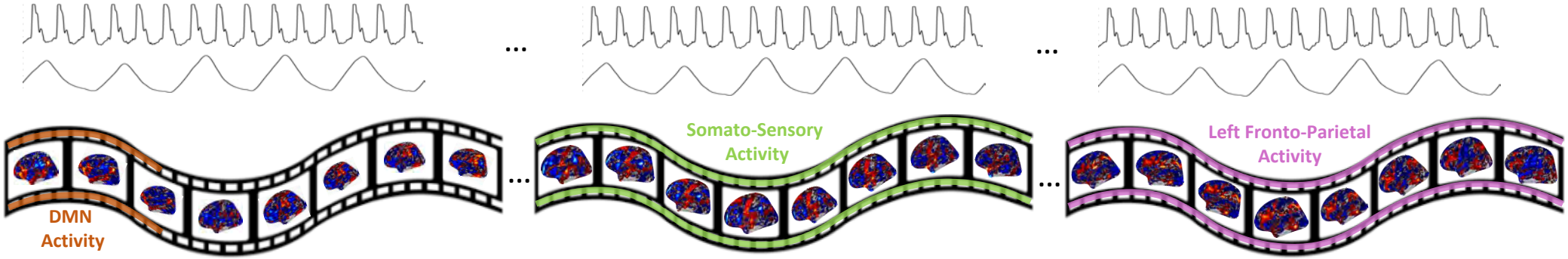
Physiology

"Neuronal"

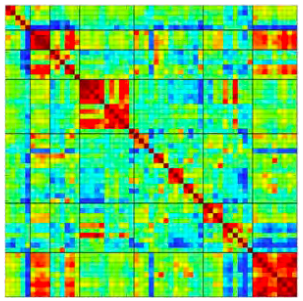
MISSING

MISSING

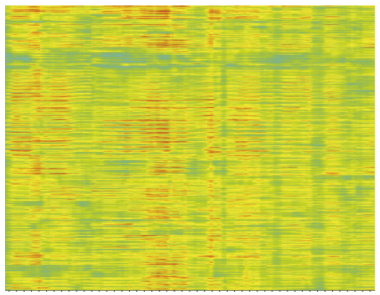
MISSING



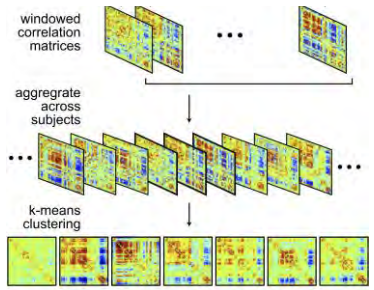
Static FC



Dynamic FC

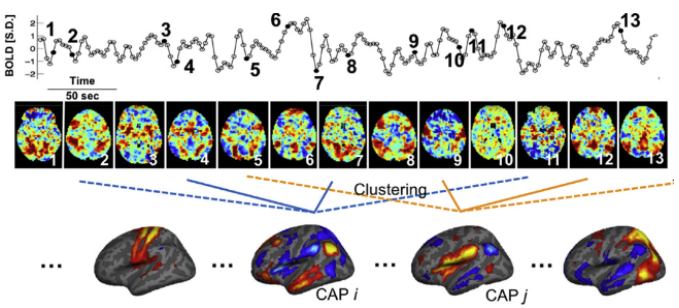


Chang et al. (2010); Leonardi et al. (2013)



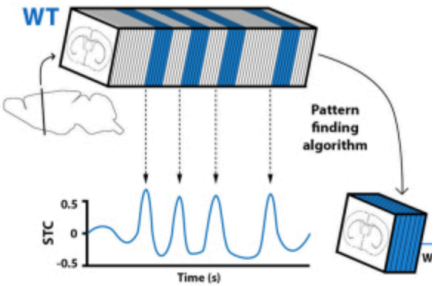
FC STATES

Allen et al. (2014);
Gonzalez-Castillo et al. (2015)



CO-ACTIVATION PATTERNS (CAPs)

Xiao et al. (2013); Bolton et al. (2020); Tagliazucchi et al. (2012)



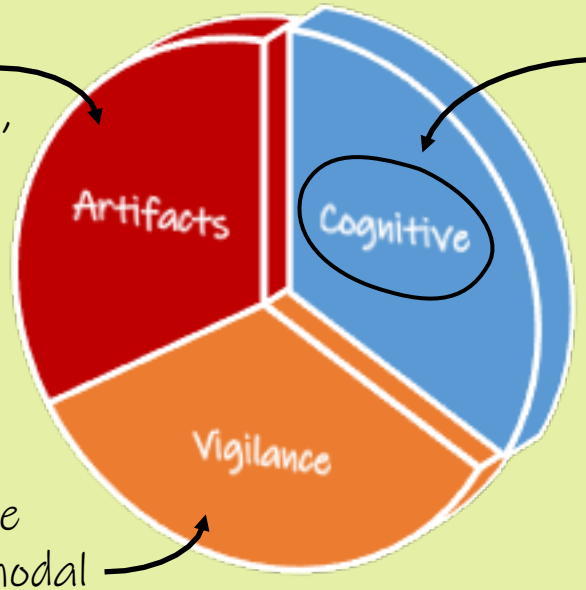
QUASI-PERIODIC PATTERNS

Yousefi et al. (2018); Belloy et al. (2018)

Introduction - Sources of Variance in Resting-State BOLD

Variance in Resting-State BOLD

Reduce via pre-processing, appropriate methods, sample selection

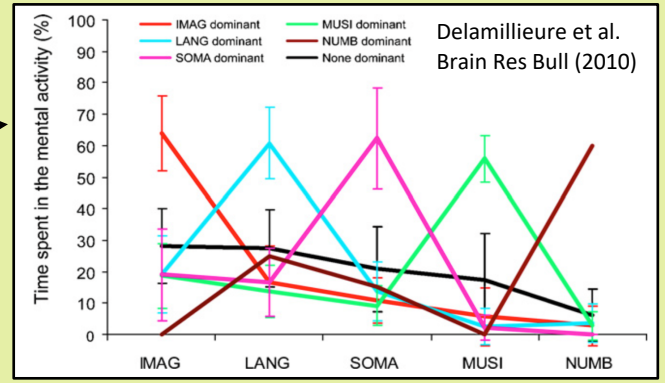


Reduce via sample selection and multi-modal imaging

What do subjects do when we ask them to lie still in the scanner and let their mind wander?

* Engage in stimuli independent thoughts
  * Inner speech
  * Inner seeing
  * Unsymbolized thinking
  * Feelings
* Have periods of sensory awareness
  * Visual
  * Auditory
  * Tactile
* General house-keeping functions

There is significant inter-subject variability in the distribution of inner experiences subjects have in the scanner.



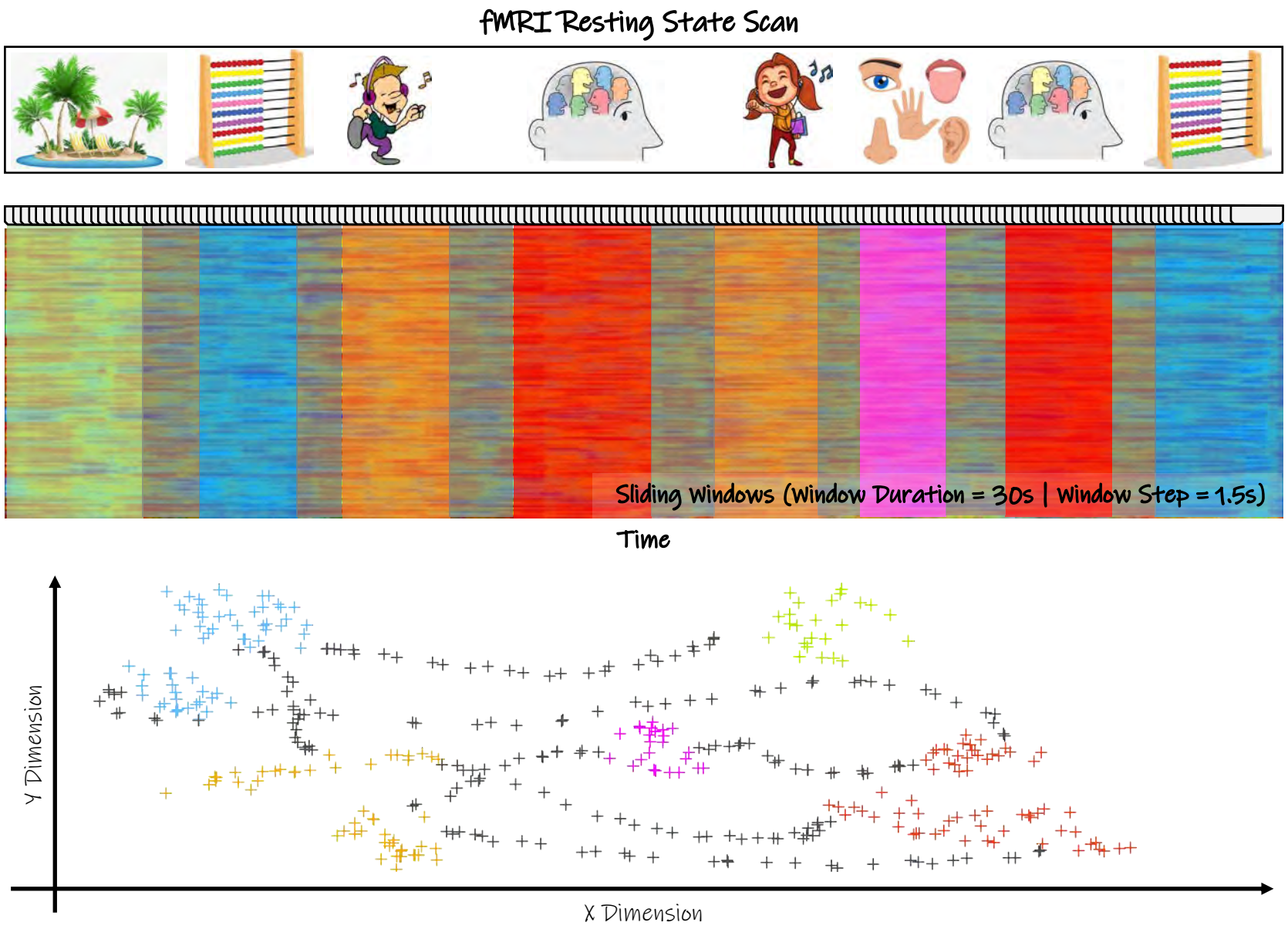
Delamillieure et al. Brain Res Bull (2010)

Linking dynamic FC to ongoing cognition – Methods Development: Framework

Mental Life Perspective

Dynamic FC Perspective

Low Dimensional Representation



Gonzalez-Castillo et al. NeuroImage (2019)

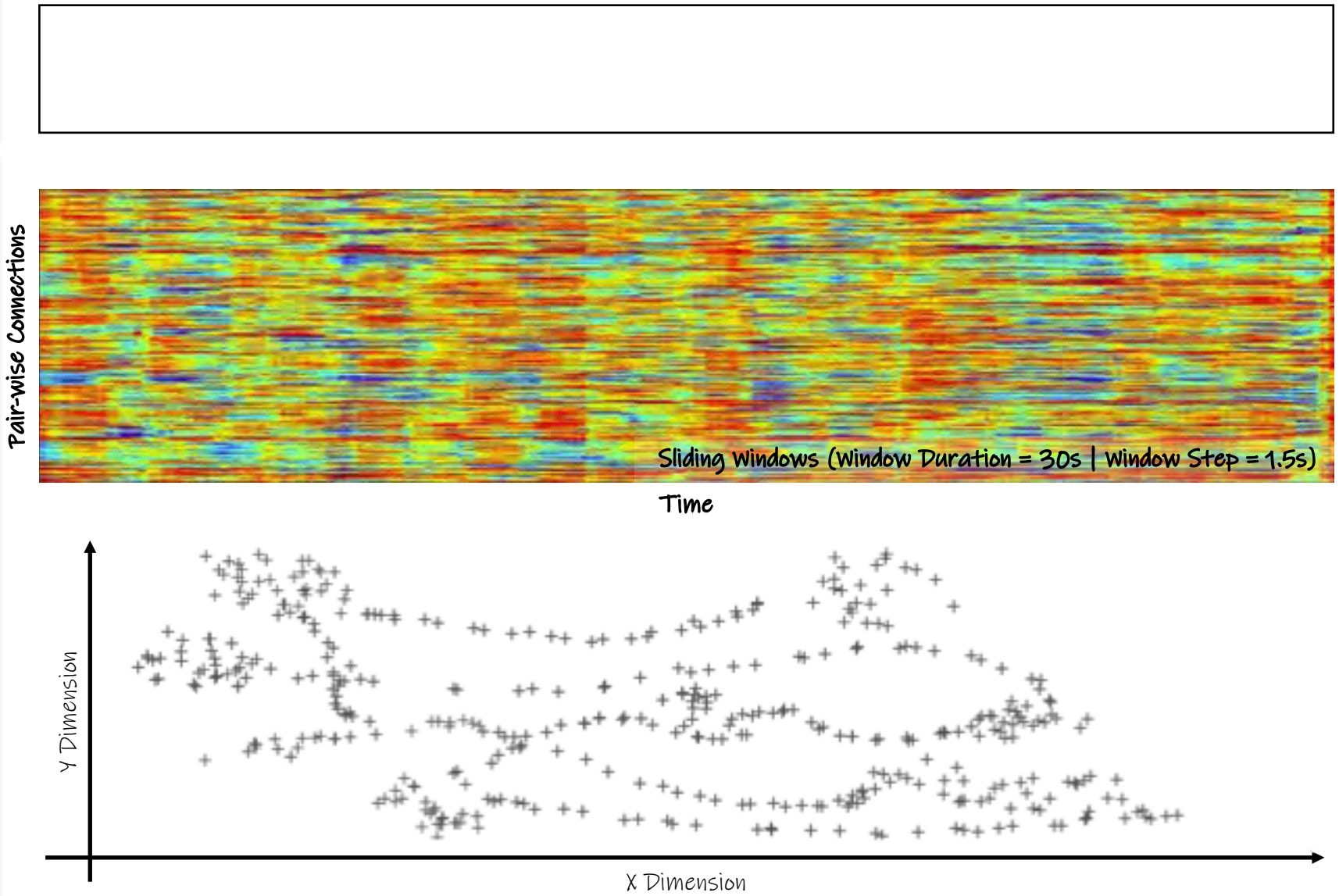
Linking dynamic FC to ongoing cognition – Methods Development: Framework

Mental Life Perspective

Dynamic FC Perspective

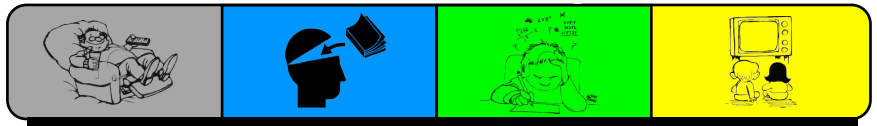
Low Dimensional Representation

fMRI Resting State Scan



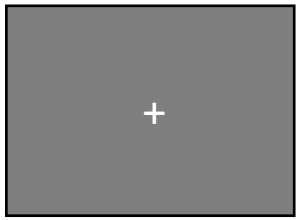
Gonzalez-Castillo et al. NeuroImage (2019)

Multi-Task Dataset | Testing



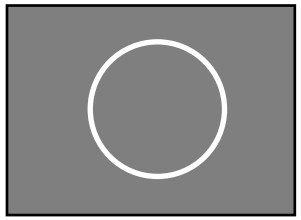
Continuous Rest Dataset | Application

REST



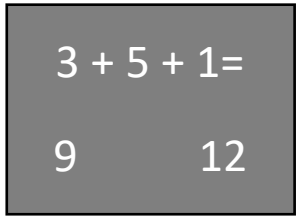
Passively fixate on the crosshair on the center of the screen

MEMORY



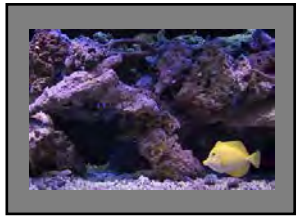
Press button when shape in screen is same as two before.

MATH



Select the correct answer from the two available options.

VIDEO



Press button when cross hair is over fish (2 options)

20 Subjects | 7T | 2x2x2 mm^3 | TR = 1.5s

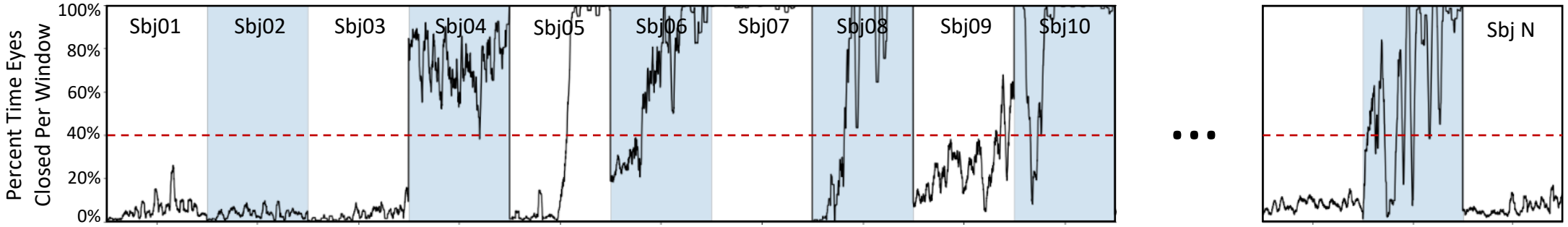
Gonzalez-Castillo et al. PNAS 2015

Linking dynamic FC to ongoing cognition – Methods Development: Datasets

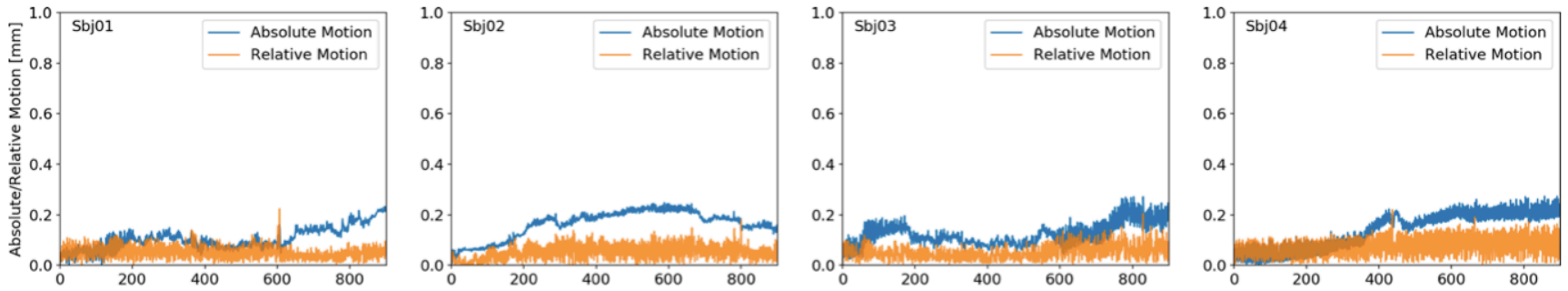
Multi-Task Dataset | Testing

Continuous Rest Dataset | Application

- 175 Subjects, each with four 15-min long, eyes-open resting state scans with concurrent eye tracking recordings.
- Subjects that stayed awake during the whole rest scan (based on eye tracking traces).



- Of these, we focused on the 20 subjects with the least amount of motion.

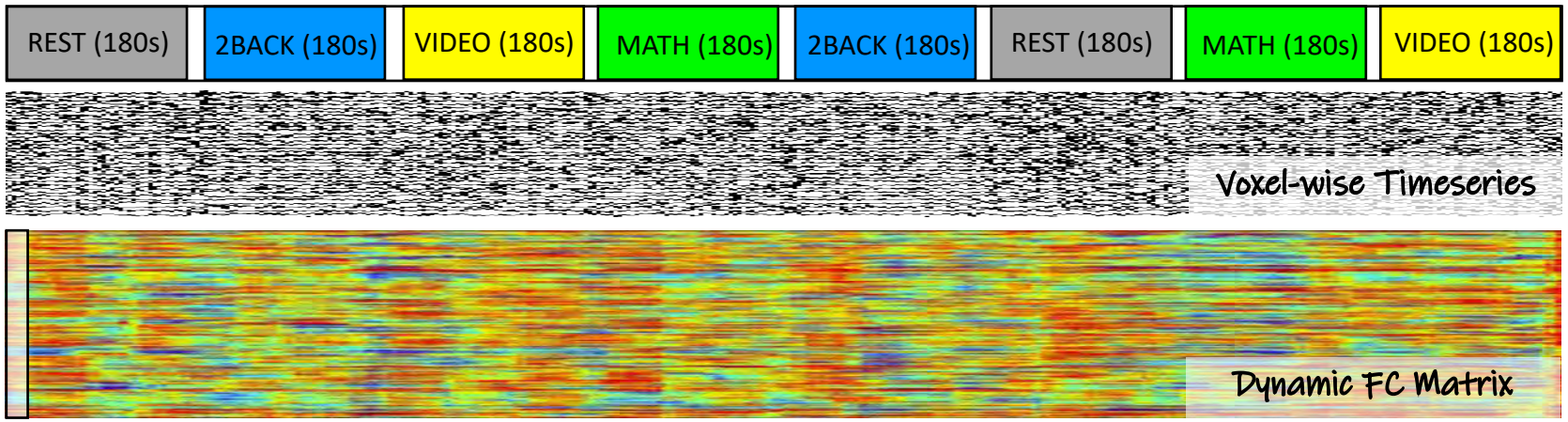


Average absolute motion was 0.27 ± 0.18 mm, and average relative volume-to-volume motion was 0.10 ± 0.07 mm.

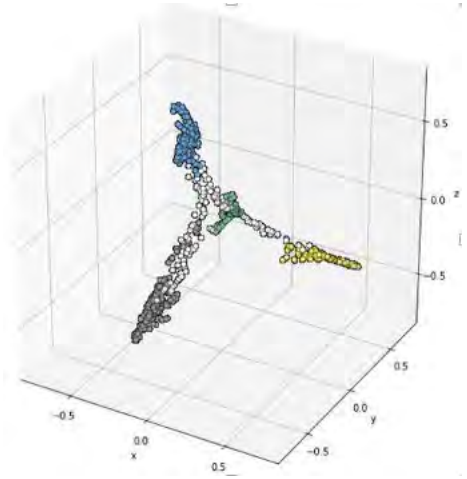
Van Essen et al. NeuroImage 2013

Linking dynamic FC to ongoing cognition – Methods Evaluation on Multi-Task Dataset

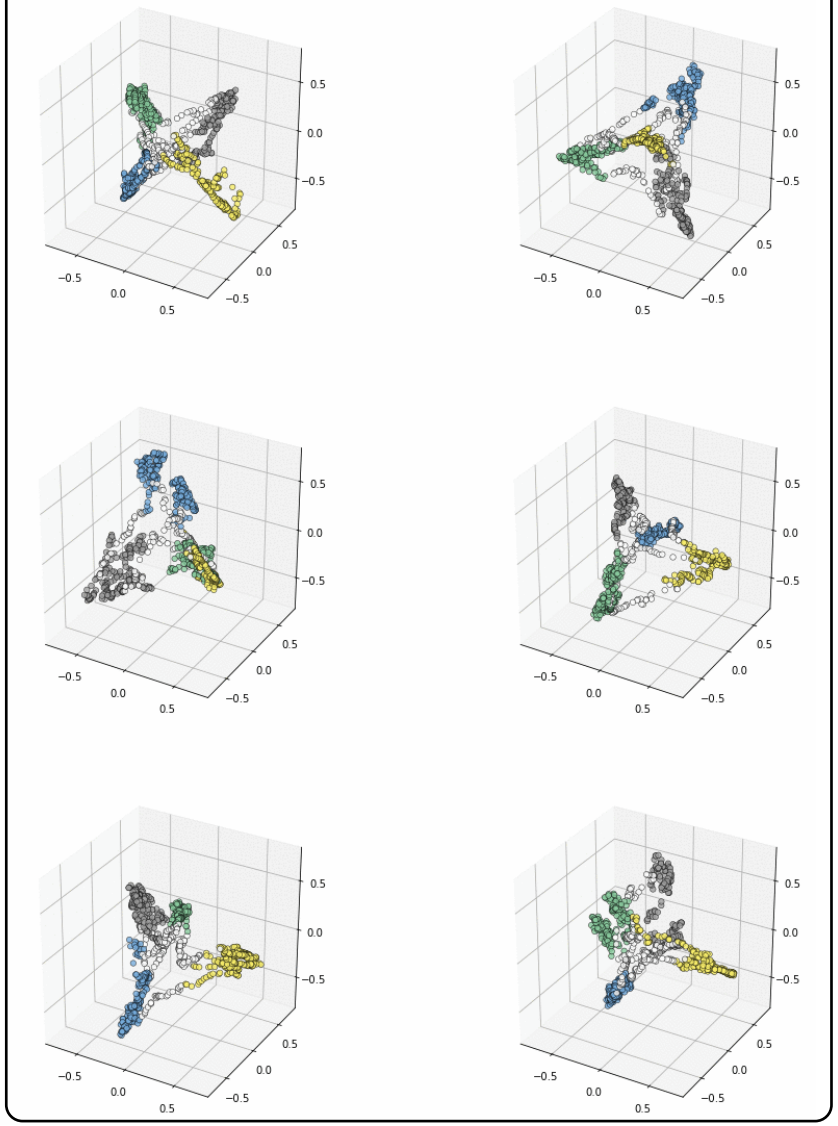
Section on Functional Imaging Methods



1. Generate Low Dimensional Representations of dFC Matrix



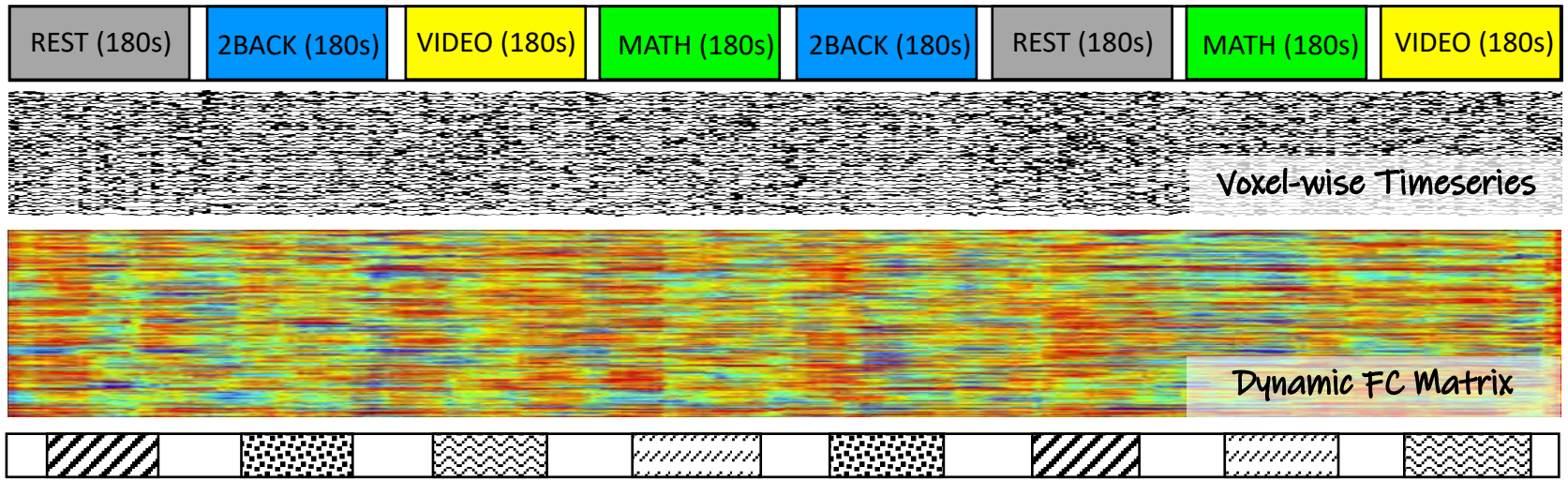
Embeddings for representative subjects



Gonzalez-Castillo et al. NeuroImage (2019)

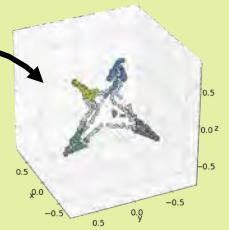
Linking dynamic FC to ongoing cognition – Methods Evaluation on Multi-Task Dataset

Section on Functional Imaging Methods



Low dimensional plots of dFC carry info about cognitive processes (at least, those dictated by tasks)

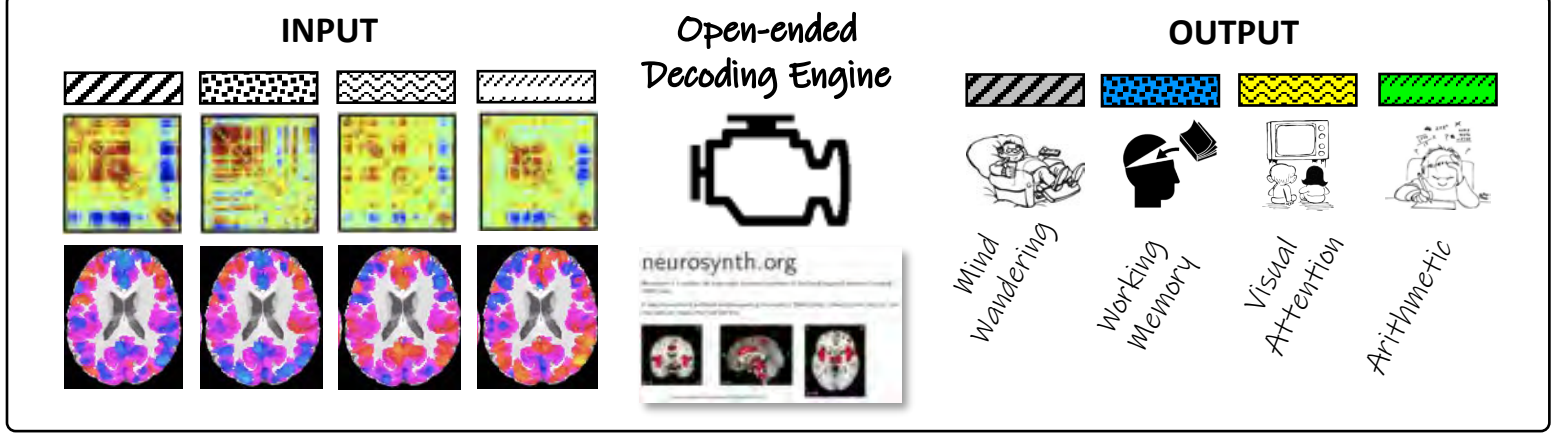
Distinct mental activities sit at corners of the embeddings



Yet, we do not know what those activities are

Low Dimensional Embedding of dFC (Corners)

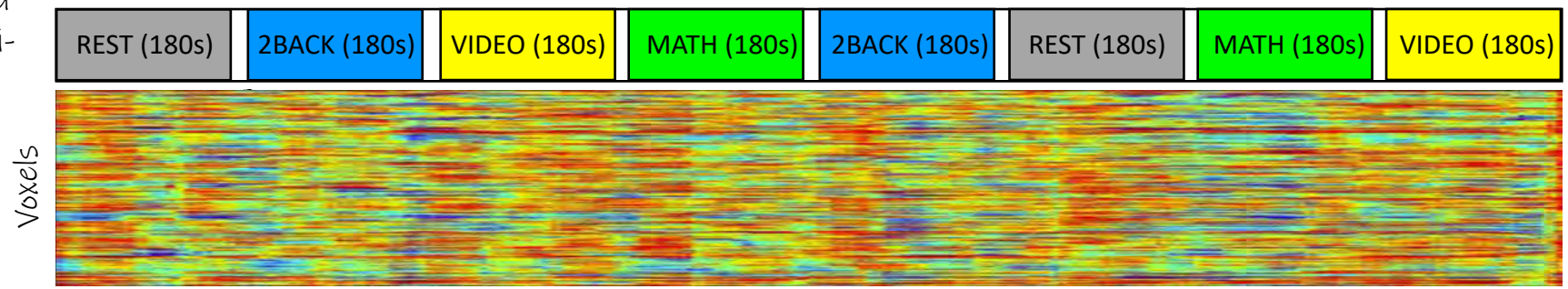
2. Decode Cognitive Processes aligned with each segment



Gonzalez-Castillo et al. NeuroImage (2019)

Linking dynamic FC to ongoing cognition – Methods Evaluation on Multi-Task Dataset

1. We switch from a dFC-view to a multi-variate activity view.



Gonzalez-Castillo et al. NeuroImage (2019)

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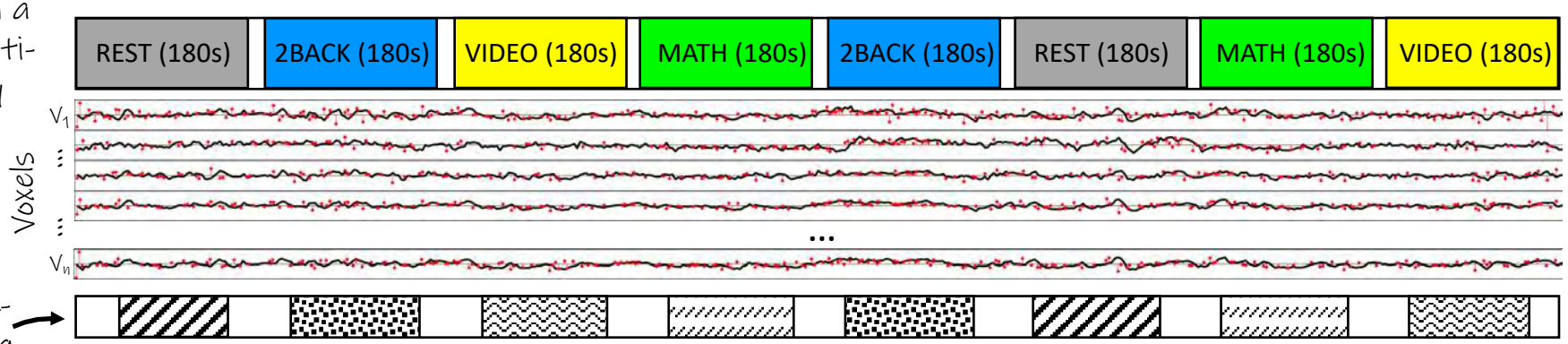
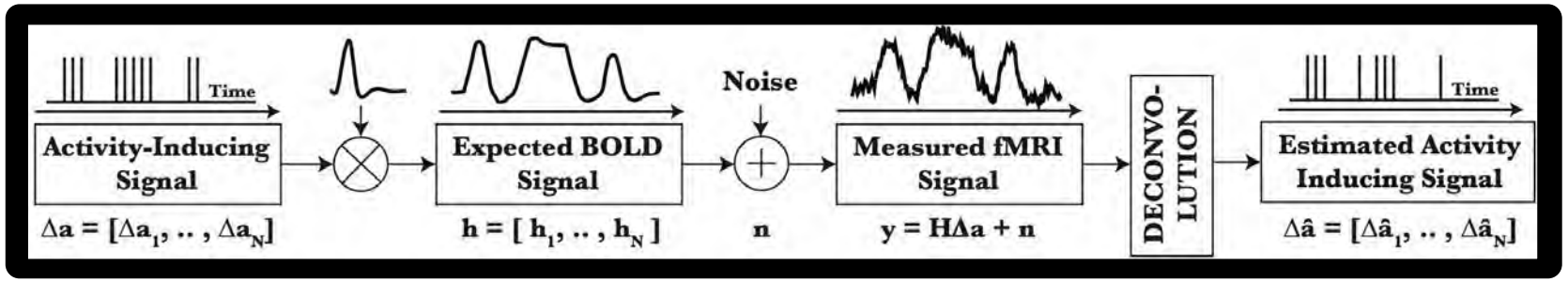


2. We apply deconvolution to find most prominent HRF-inducing events

3. We rely on the dFC-based scan partitioning.

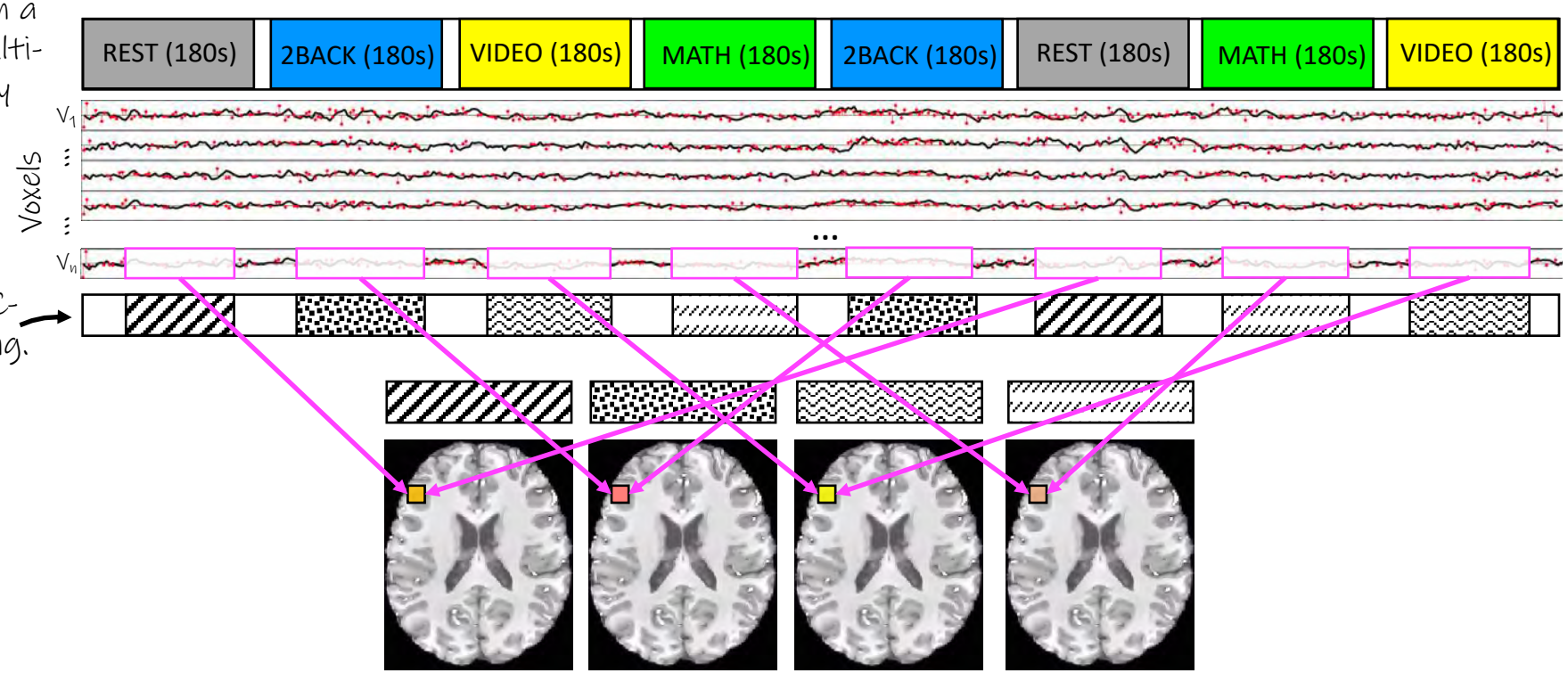


Hemodynamic Deconvolution – Find Most Prominent Activity Inducing Events
(SPFM; *Caballero-Gaudes et al. HMB 2011*)

Gonzalez-Castillo et al. NeuroImage (2019)

Linking dynamic FC to ongoing cognition – Methods Evaluation on Multi-Task Dataset

1. We switch from a dFC-view to a multivariate activity view.



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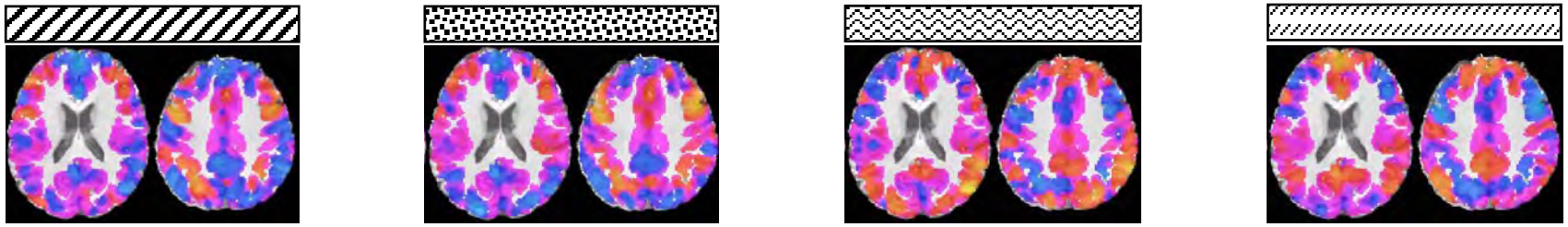


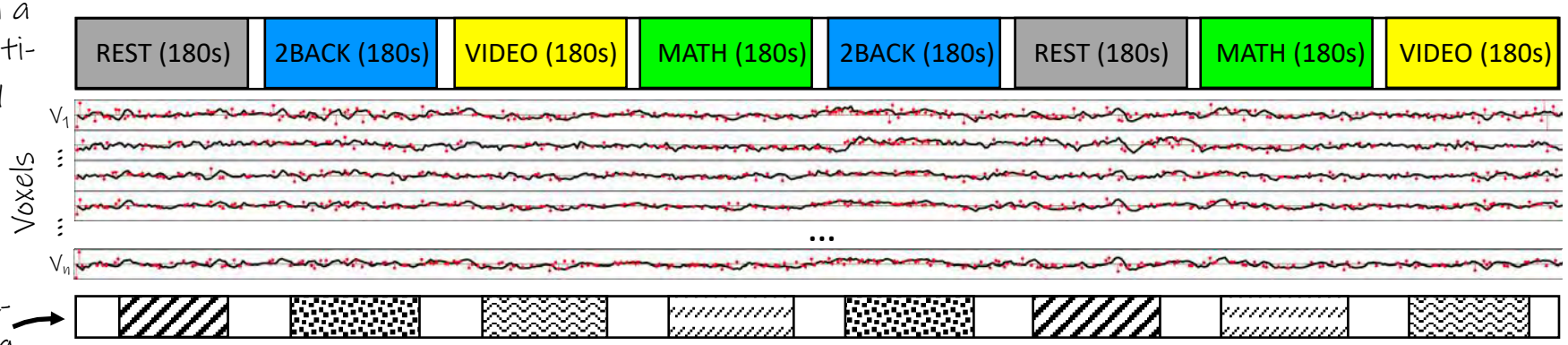
4. Create "activity" maps per segment via deconvolution

Gonzalez-Castillo et al. NeuroImage (2019)

Linking dynamic FC to ongoing cognition – Methods Evaluation on Multi-Task Dataset

Section on Functional Imaging Methods

1. We switch from a dFC-view to a multi-variate activity view.



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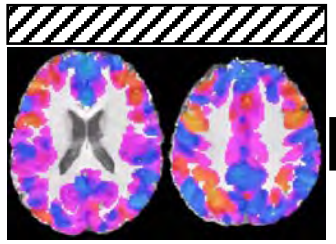

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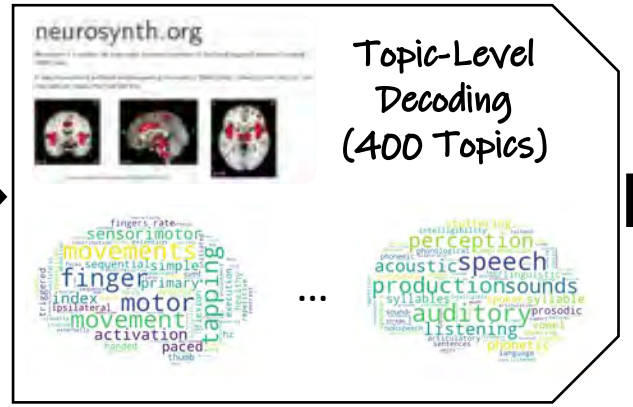
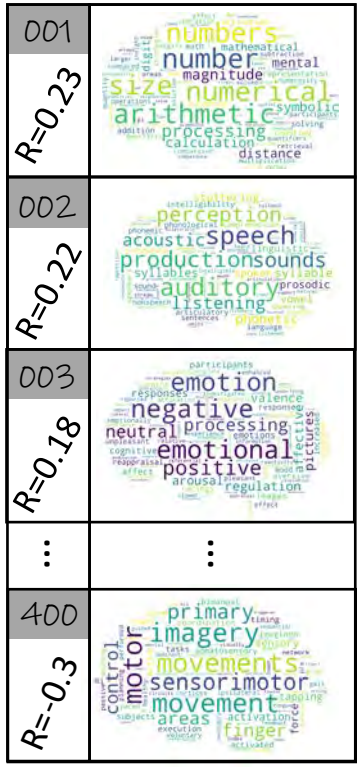
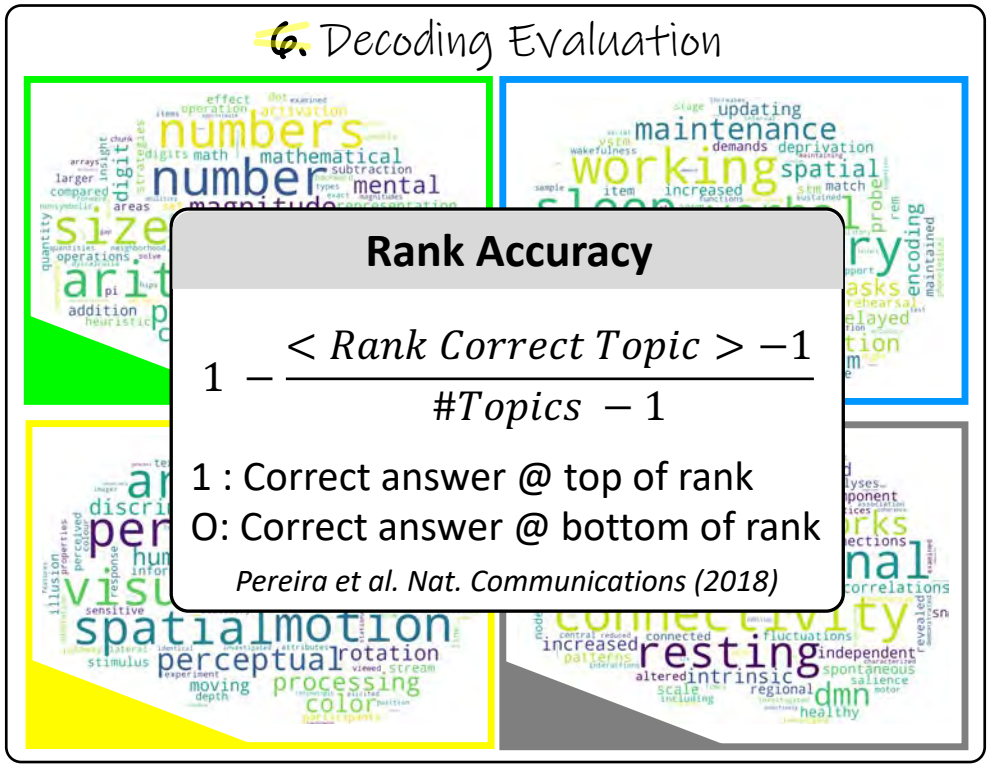


5. Use Neurosynth's reverse-inference abilities to obtain cognitive topics that most highly relate to each "activity" map



6. Decoding Evaluation



Rank Accuracy

$$1 - \frac{< Rank\ Correct\ Topic > -1}{\#Topics\ -1}$$

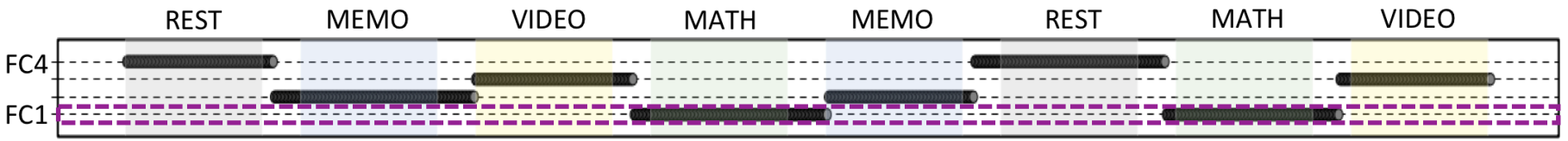
1 : Correct answer @ top of rank
O: Correct answer @ bottom of rank

Pereira et al. Nat. Communications (2018)

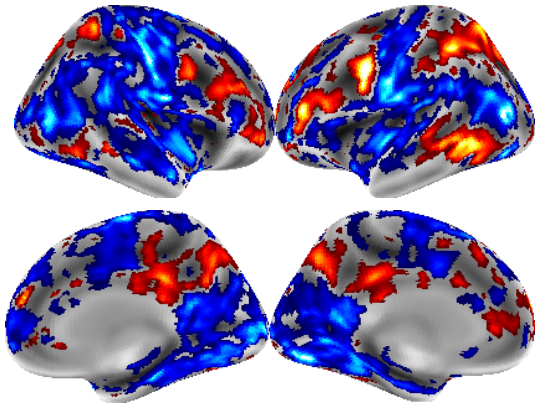
Gonzalez-Castillo et al. NeuroImage (2019)

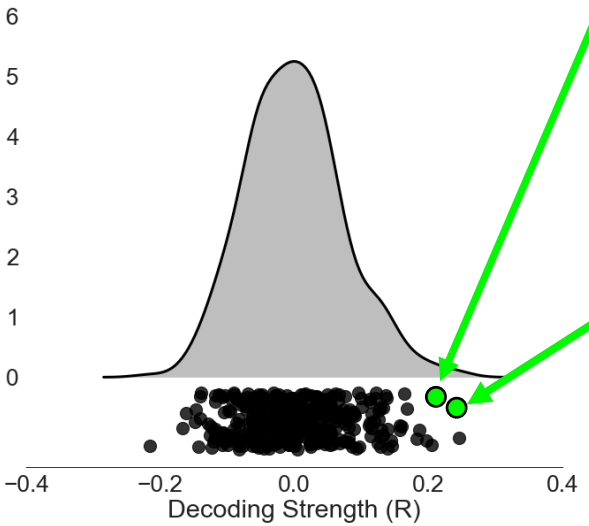
Linking dynamic FC to ongoing cognition – Methods Evaluation on Multi-Task Dataset

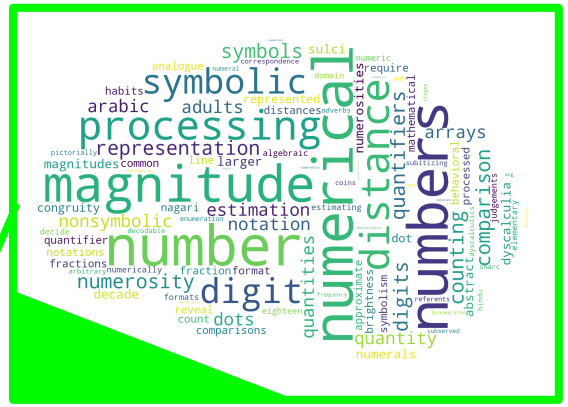
Automatic Scan Segmentation
based on dynamic-FC

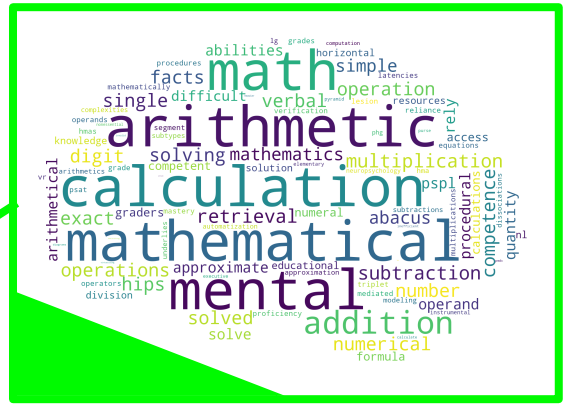


"Activity" Map
for FC1





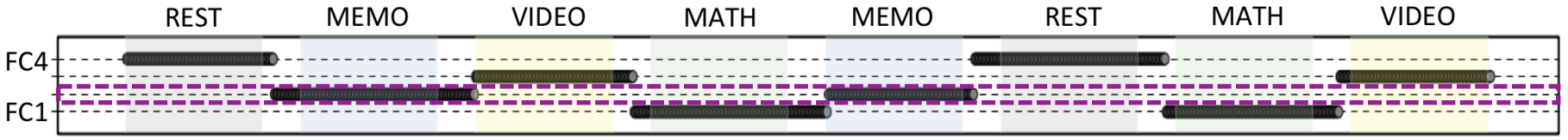




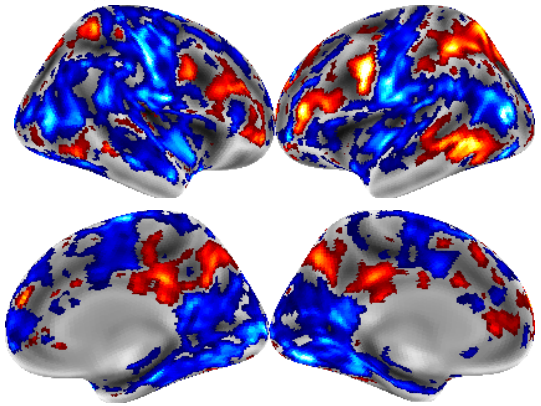
Gonzalez-Castillo et al. NeuroImage (2019)

Linking dynamic FC to ongoing cognition – Methods Evaluation on Multi-Task Dataset

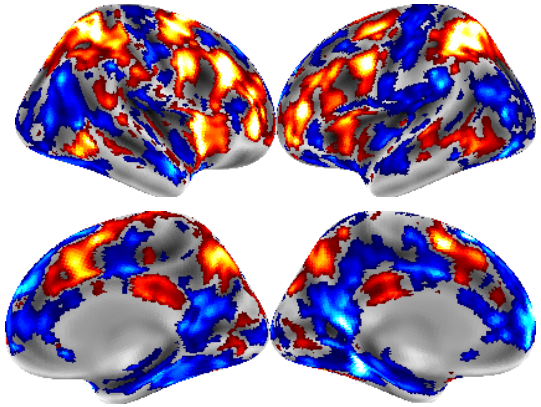
Automatic Scan Segmentation
based on dynamic-FC

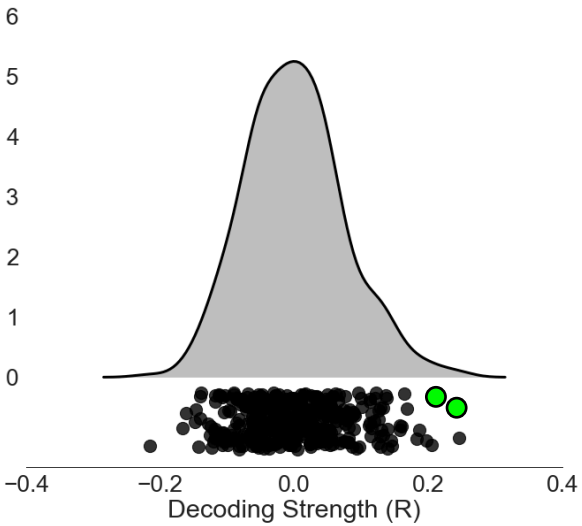


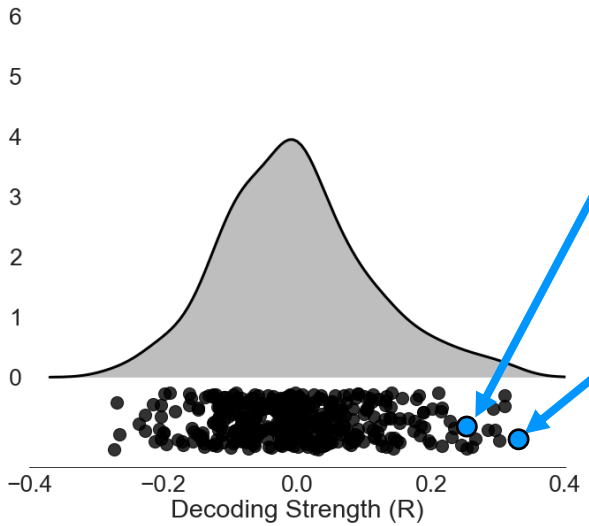
"Activity" Map
for FC1



FC2 – "Activity" Map







Gonzalez-Castillo et al. NeuroImage (2019)

Linking dynamic FC to ongoing cognition – Methods Evaluation on Multi-Task Dataset

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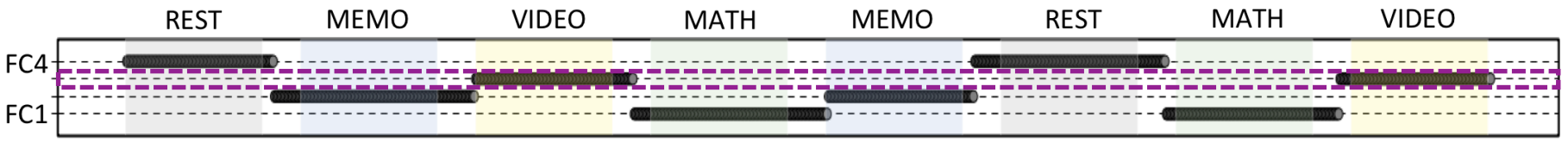
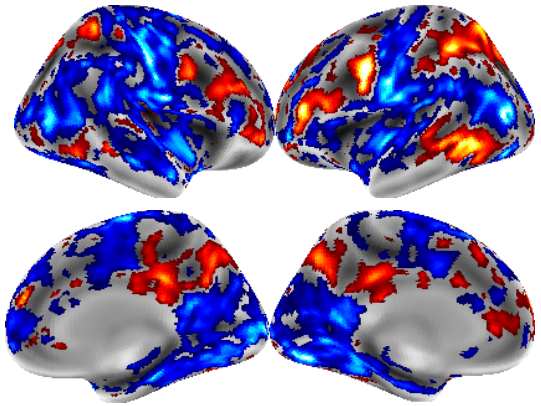


"Activity" Map for FC1



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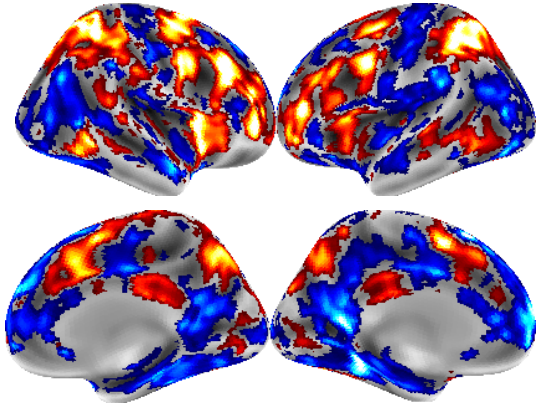

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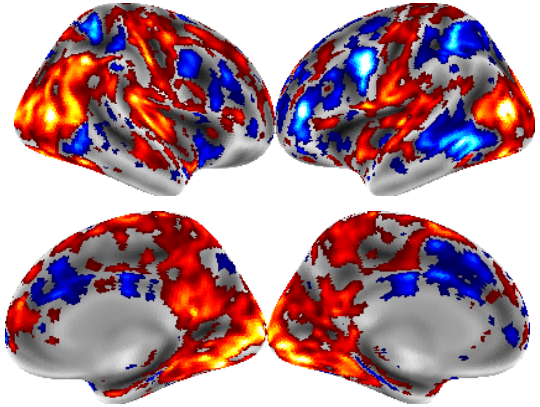

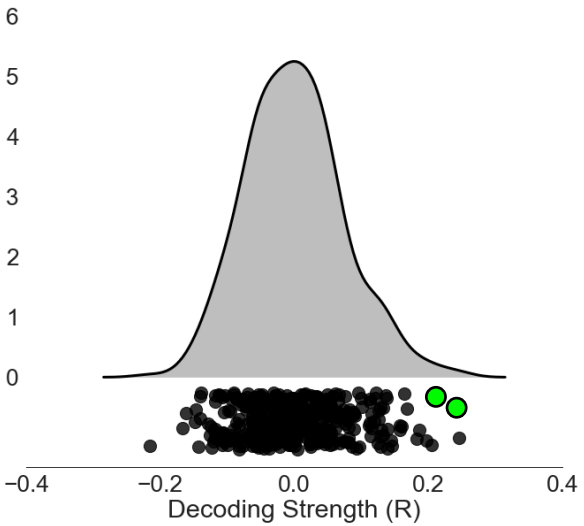

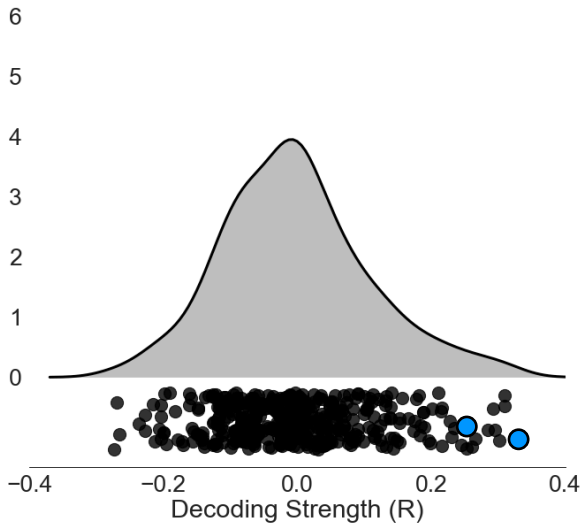

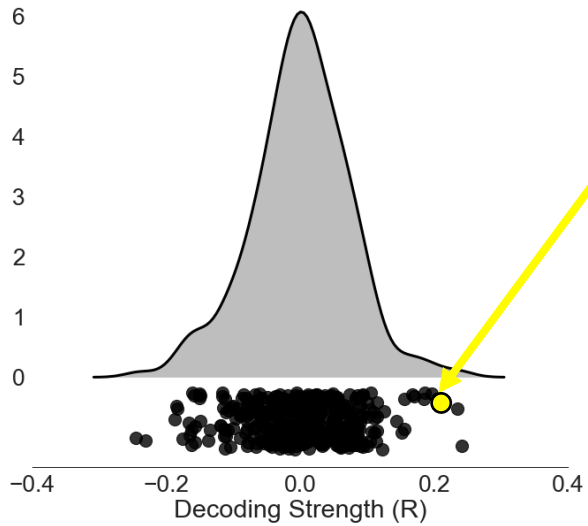

Gonzalez-Castillo et al. NeuroImage (2019)

Linking dynamic FC to ongoing cognition – Methods Evaluation on Multi-Task Dataset

Section on Functional Imaging Methods

Automatic Scan Segmentation
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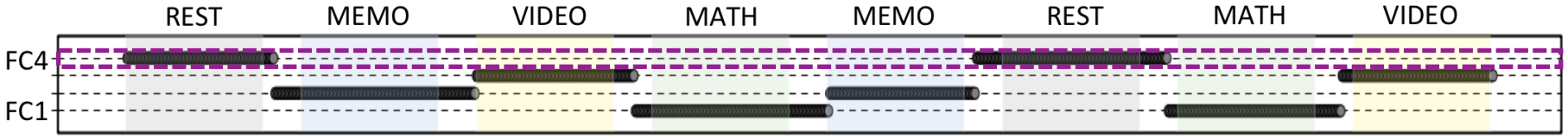

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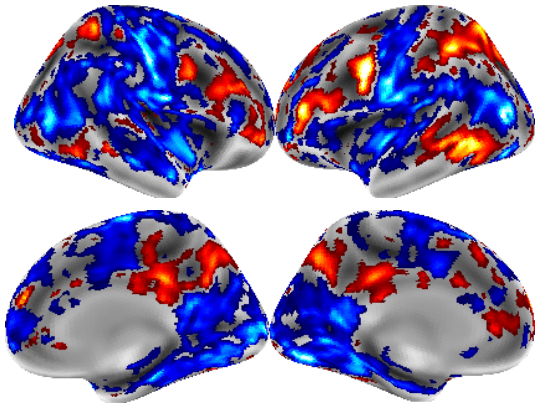
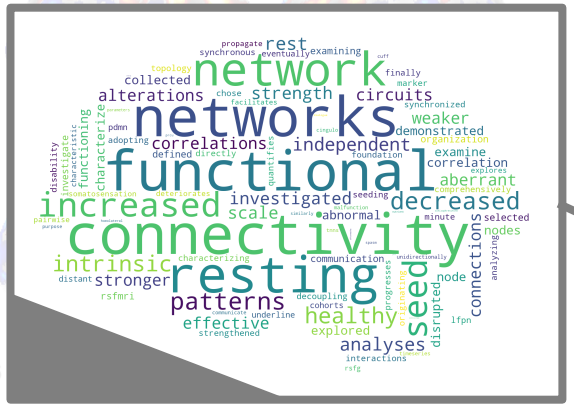
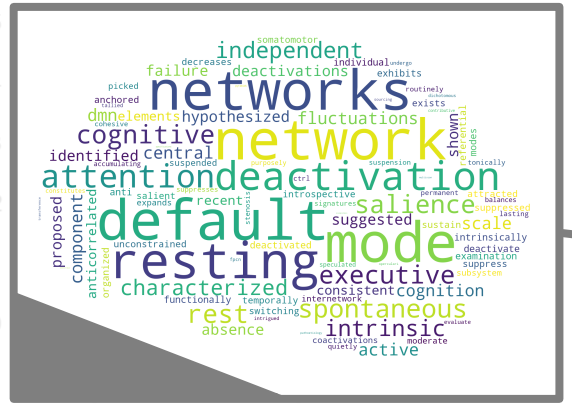
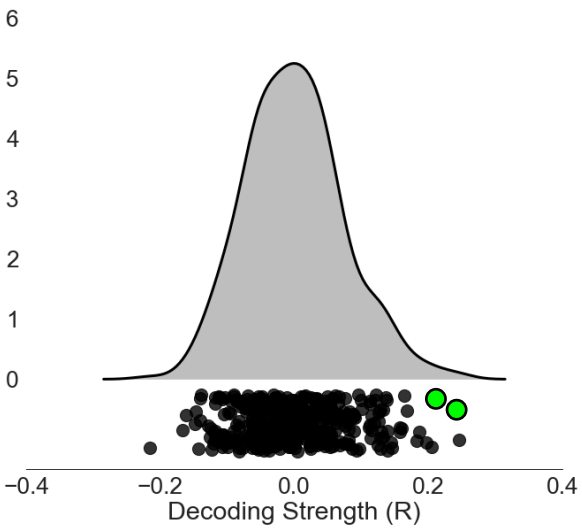
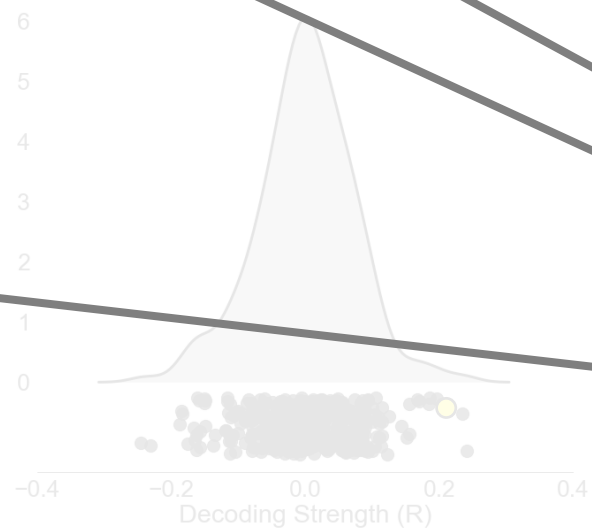


FC2 – "Activity" Map

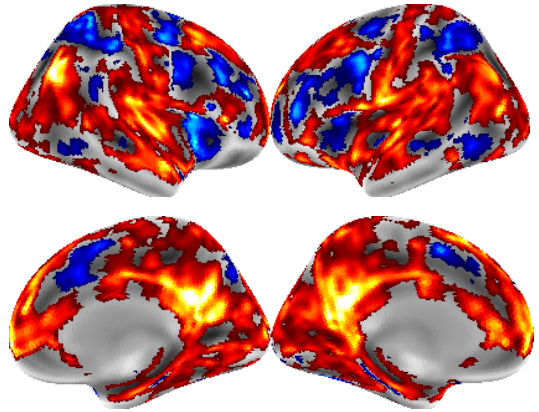


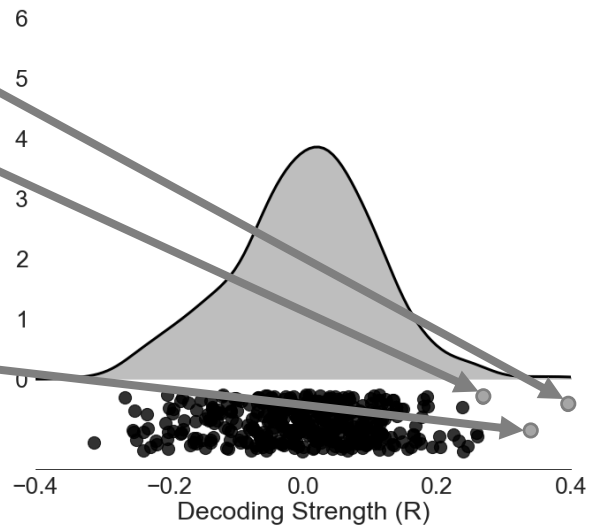






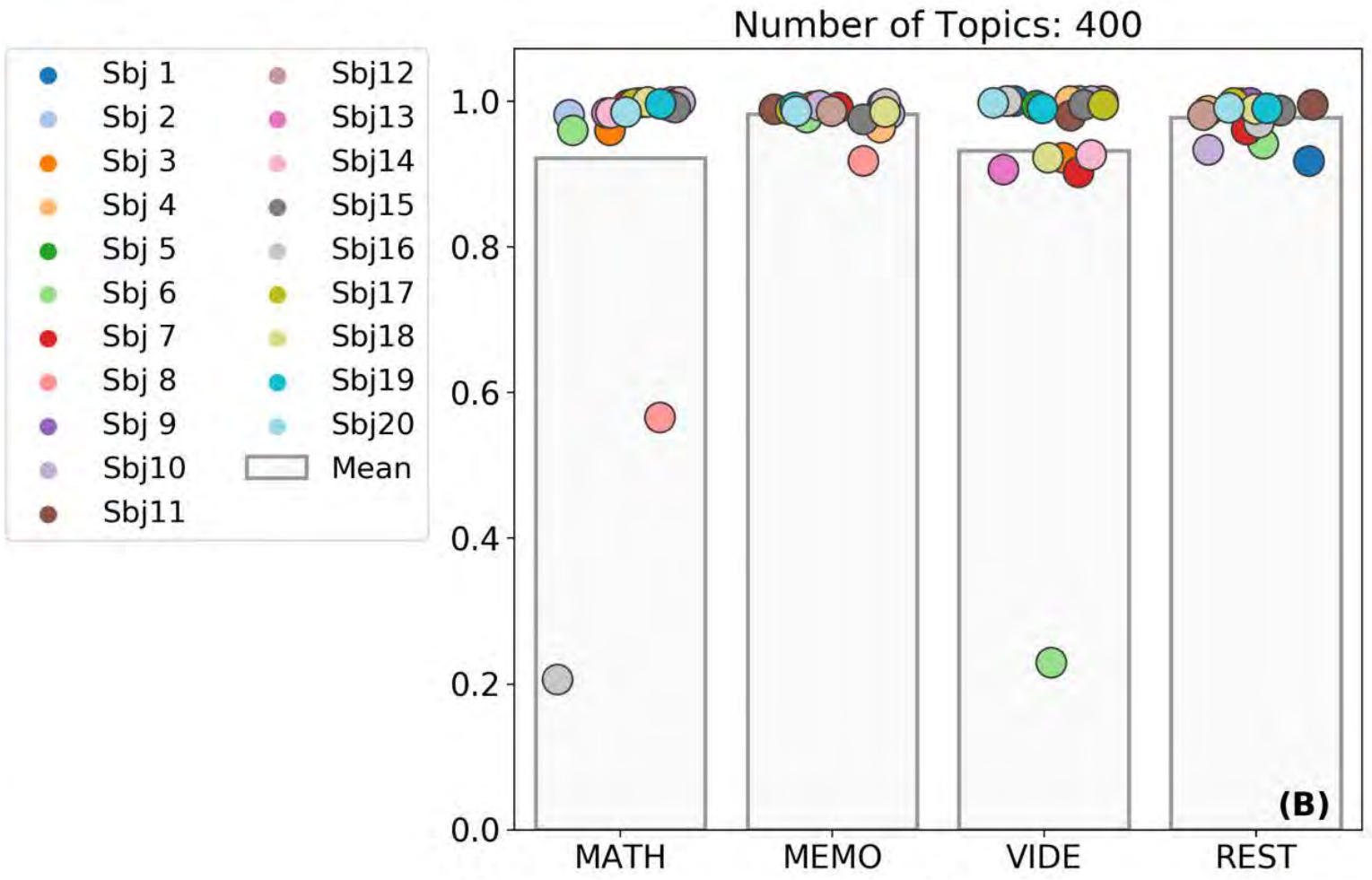
FC4 – "Activity" Map





Linking dynamic FC to ongoing cognition – Methods Evaluation on Multi-Task Dataset

Group Level Decoding Accuracy Results



Rank Accuracy

$$1 - \frac{< Rank\ Correct\ Topic > -1}{\#Topics\ - 1}$$

1 : Correct answer @ top of rank

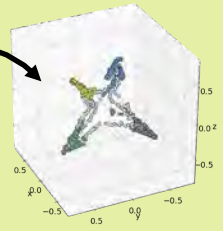
O: Correct answer @ bottom of rank

Pereira et al. Nat. Communications (2018)

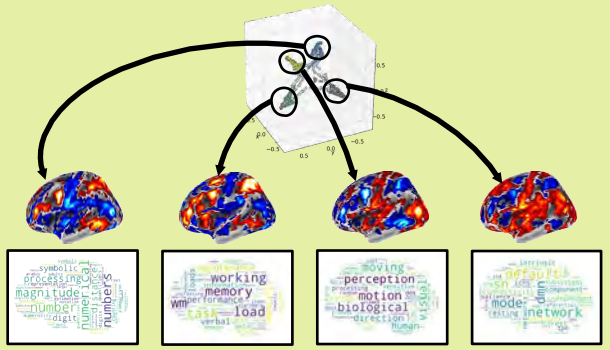
Linking dynamic FC to ongoing cognition – Application to Resting-State Dataset

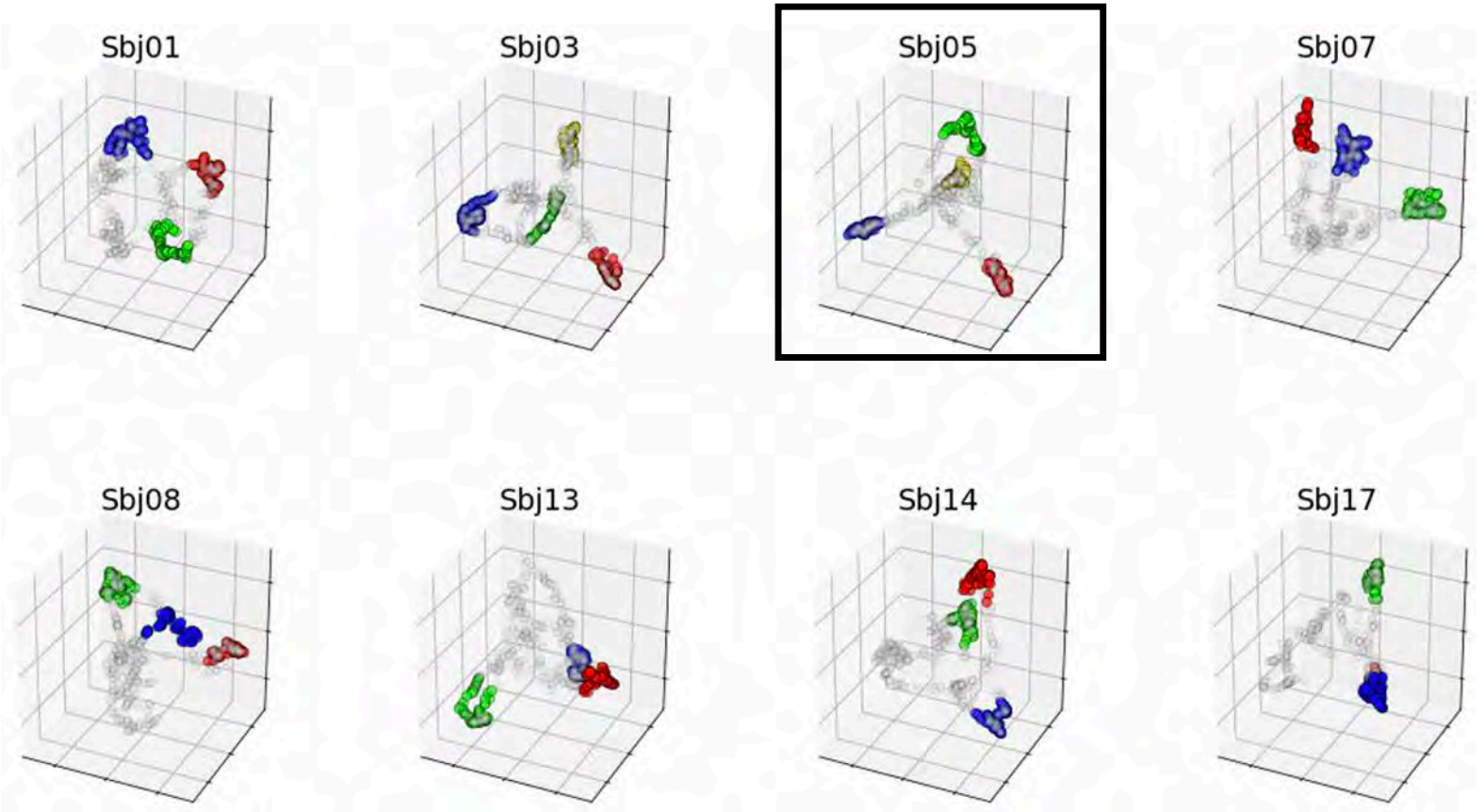
- Low dimensional plots of dFC carry info about cognitive processes (at least, those dictated by tasks)

Distinct mental activities sit at corners of the embeddings

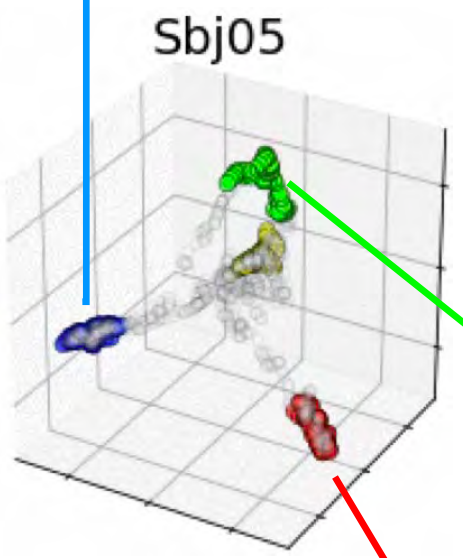


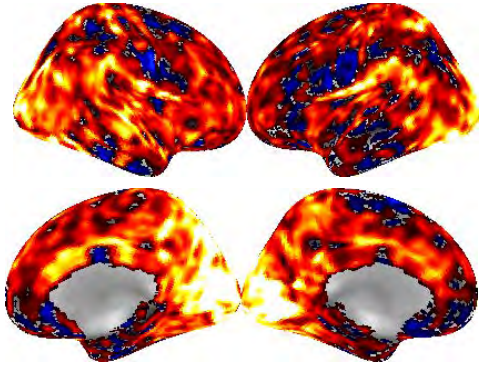
- Deconvolution + Neurosynth to infer the nature of the main cognitive processes ongoing during each segment

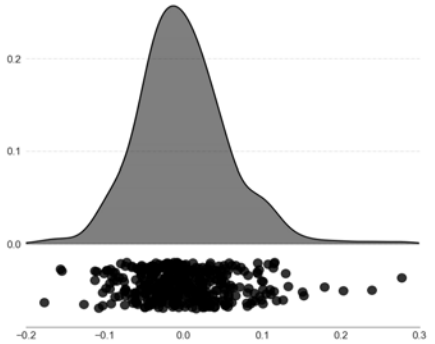




Linking dynamic FC to ongoing cognition – Application to Resting-State Dataset

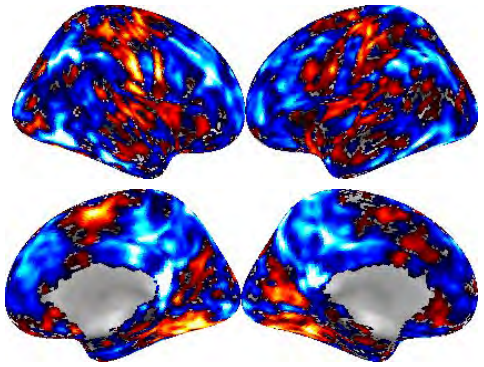


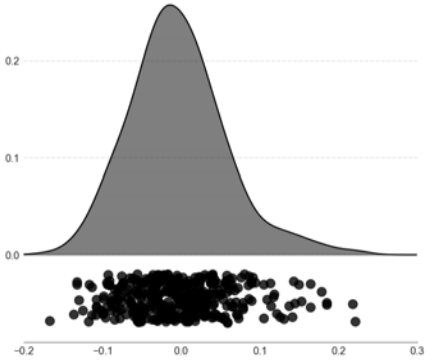




TOP 5 TOPICS

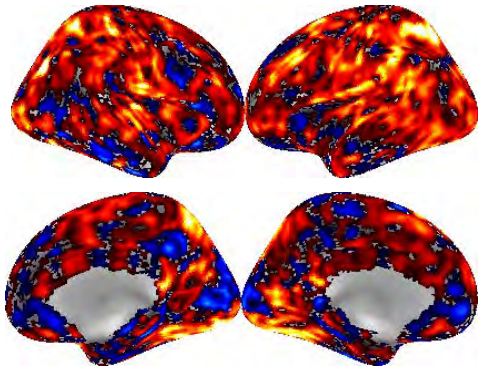
0.28	Visual, areas, stimulus,…
0.24	Blind, visual, sighted,…
0.20	Motion, biological, moving, …
0.18	Shape, shapes, texture, …
0.15	Stream, visual, streams, …

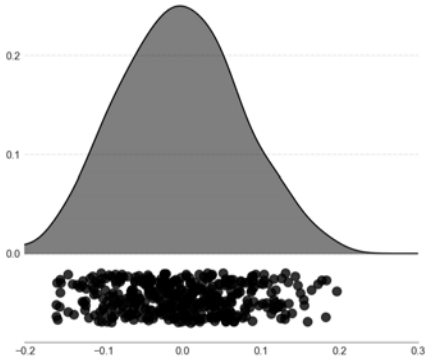




TOP 5 TOPICS

0.22	Motor, sensory, areas, …
0.22	Motor, finger, movements, …
0.19	Movement, movements, motor, …
0.19	Touch, tactile, somatosensory, …
0.18	Stimulation, somatosensory, tactile, …





TOP 5 TOPICS

0.20	Task, tasks, matching, …
0.18	Arithmetic, calculation, mathematical, …
0.18	Spatial, location, locations, …
0.18	Number, numerical, numbers, …
0.17	Action, actions, observation, …

Linking dynamic FC to ongoing cognition – Application to Resting-State Dataset

* At the group level, only 78 topics (out of 400) were marked as significant outliers (right tail).

* Of those 78, very few appeared as significant in multiple occasions (e.g., different spikes)

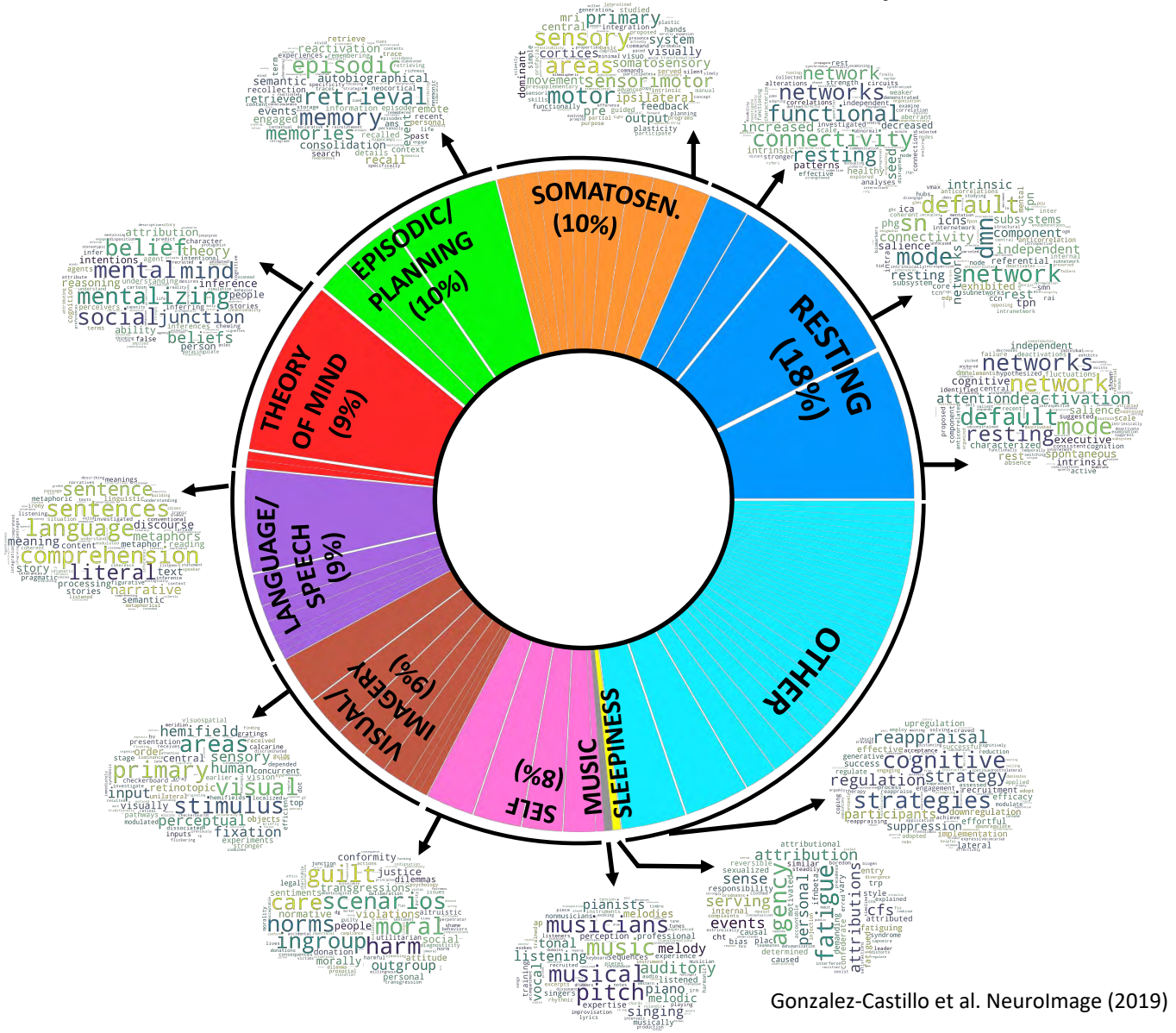
INTERIM CONCLUSIONS

* Data-driven estimates of covert cognition agree with previous reports of what are the most common mental activities subjects perform during rest.

* *"dFC + Deconvolution + Neurosynth"* can help us uncover the cognitive correlates of distinct dFC patterns during task and rest.

* Dynamic FC is modulated by covert cognition during rest

Top 15 topics most often found as associated with corners in dynamic FC Embeddings



Gonzalez-Castillo et al. NeuroImage (2019)

Linking dynamic FC to ongoing cognition – Problem solved? Umm, not really.

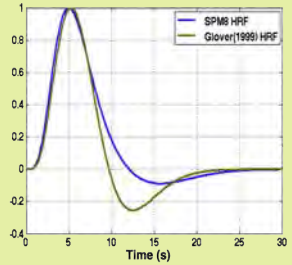
* We cannot evaluate the accuracy of individual guesses (decoding events)

* Validation / Decoding always through the lens of task-results:
  - NeuroSynth is built using results from task-based studies
  - Differences in HRF between rest and task
  - Uncertainties in interpretation
    - Visual attention vs. Visual imagery
    - Overlap with unconscious brain activity

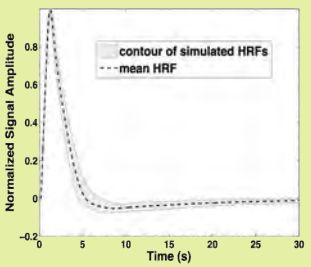
- Limited specificity of Topics
- Vocabulary biases
- Inability to incorporate priors to contextualize predictions
- Most sampled studies are task-studies

Rubin et al. (2017); Yarkoni et al. (2011)

Task HRF



Rest HRF



Glover, Chang (2015)

* Best-case scenario, we likely only captured most prominent "events/periods":
  - Missed a lot of important information needed to fully understand the joint dynamics of brain and "mind" during rest.

Linking dynamic FC to ongoing cognition – Future Steps

"Third-Person Neuroscience"

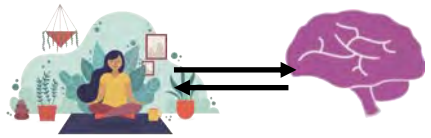
Empirical Investigations of Brain States in the third-person perspective

"First-Person Mentoscience"

Scientific Investigation of Mental States in first-person perspective in isolation from Brain States

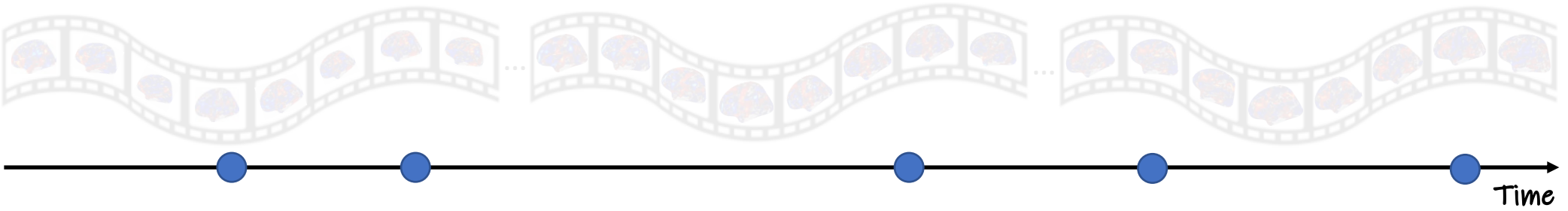
"First-Person Neuroscience"

Linking systematic examinations of mental states with data about neuronal states



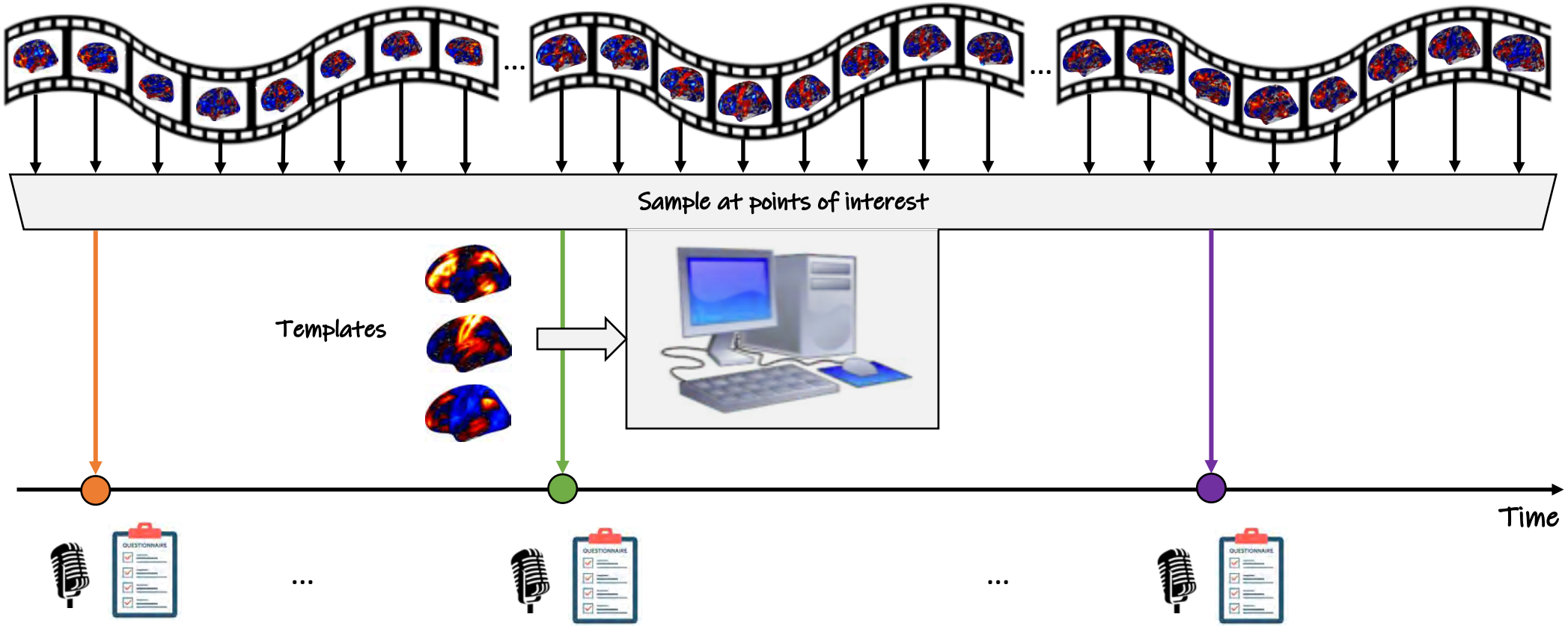
Northoff and Heinzel (2006)

Linking dynamic FC to ongoing cognition – Future Steps



Sample at random periods

Linking dynamic FC to ongoing cognition – Future Steps



Obtain an unconstrained description of mental life [zero assumptions hard to analyze]

Obtain description of mental life across pre-determined dimensions [assumptions easy to analyze]

Linking dynamic FC to ongoing cognition – Conclusions

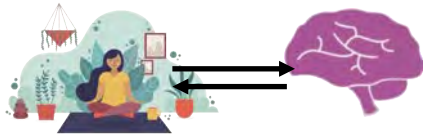
Resting State Functional Connectivity => Mean Effect **(Static Functional Connectivity)** & Small Fluctuations over the Mean **(Dynamic Functional Connectivity)**

* Since one of the original reports (Chang et al. 2010), we have made substantial progress:

- The avid debate regarding its significance (artifactual or neuronally meaningful) is starting to settle.
- Covert ongoing cognition is a modulating factor of Dynamic FC estimates.
- Reports of significant differences in dynamic FC across populations (not captured by static measures).

* Yet, there is substantial work ahead of us:

- What are the relative contributions of the different sources of variability to Dynamic FC?
- Linking brain states (dFC) and mental states will require taking into consideration first-person reports



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Gang Chen

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