Brain Network Mechanisms of Aging-Related Cognitive Decline

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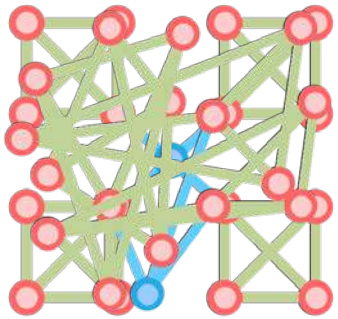
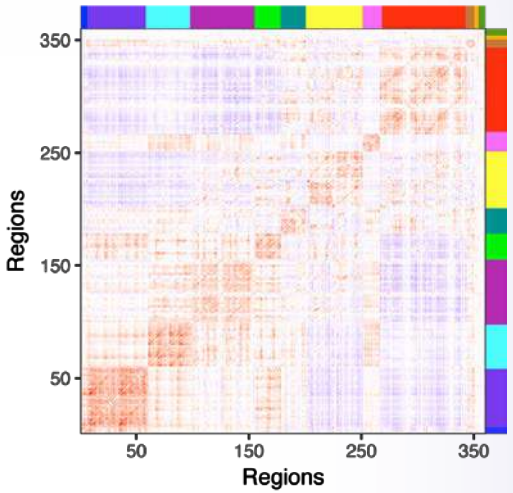
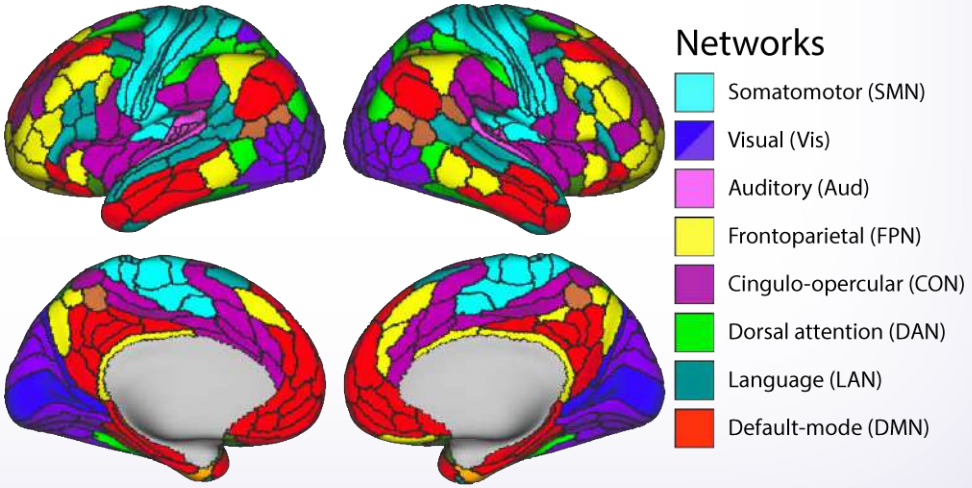
What is the brain's large-scale functional architecture?

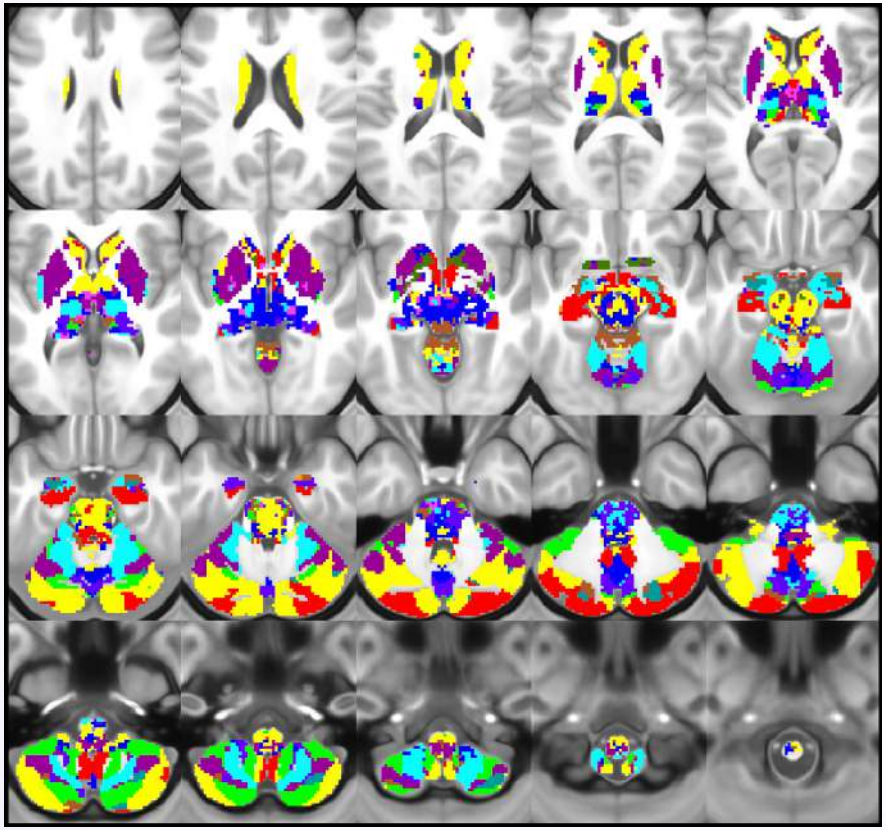
- Systems as graph communities
  - Clusters of highly interconnected nodes
- "Community detection" algorithms
- Applied to whole-brain resting-state fMRI graphs (Ji et al., in press)
  - Regions defined by Glasser et al., 2016

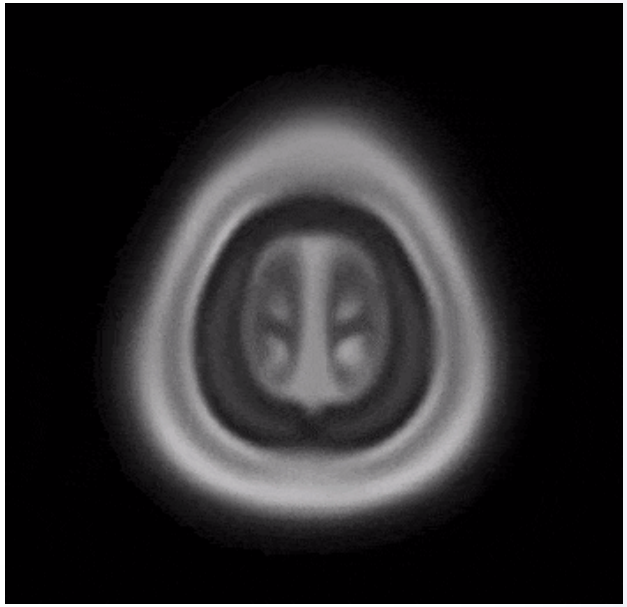






Subcortical extension of cortical networks





Available for download:
www.colelab.org/#resources

Ji et al. (In Press), *NeuroImage*

What is functional connectivity, why does it matter?

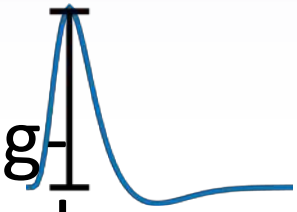
- Typical FC definition:
  "Statistical association between neural time series"
  - *What does this mean, mechanistically?*
- To the extent that FC = causal interaction between neural entities…
  - **Central to neural function, computation**
  - Neurons compute based on input **patterns**
  - No neuron acts alone
  - No million-neuron circuit acts alone
- How to make sense of large-scale FC? Analyze **patterns**
  - Graph theory (e.g., hubs, communities),
    machine learning (link activity/FC patterns to cognition)

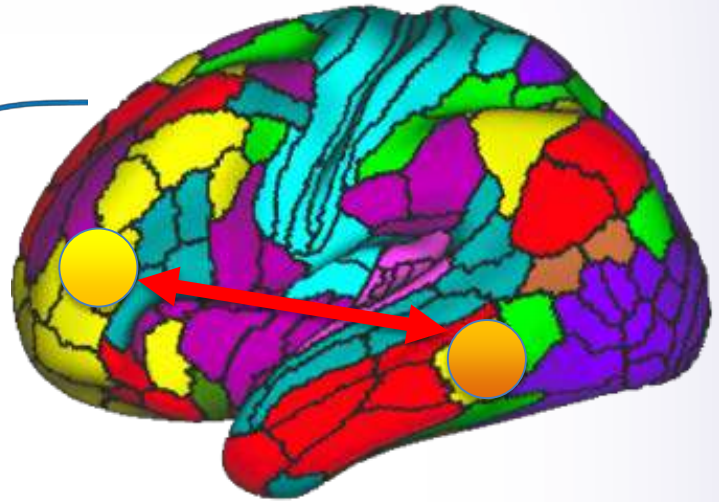
Overview

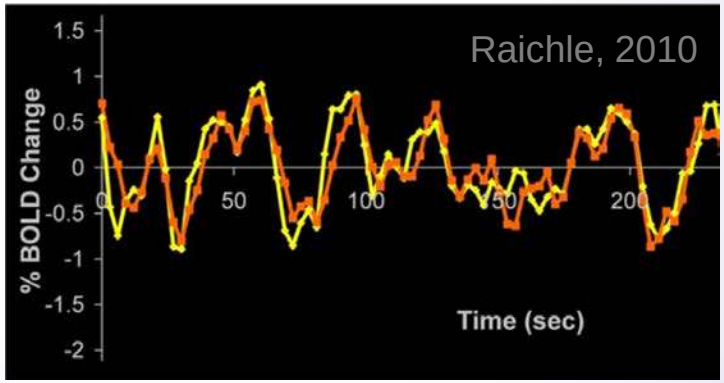
1. Cognitive activations spread via resting-state FC topology
2. Predicting unhealthy aging-related cognitive activation changes

Resting-state FC and cognition

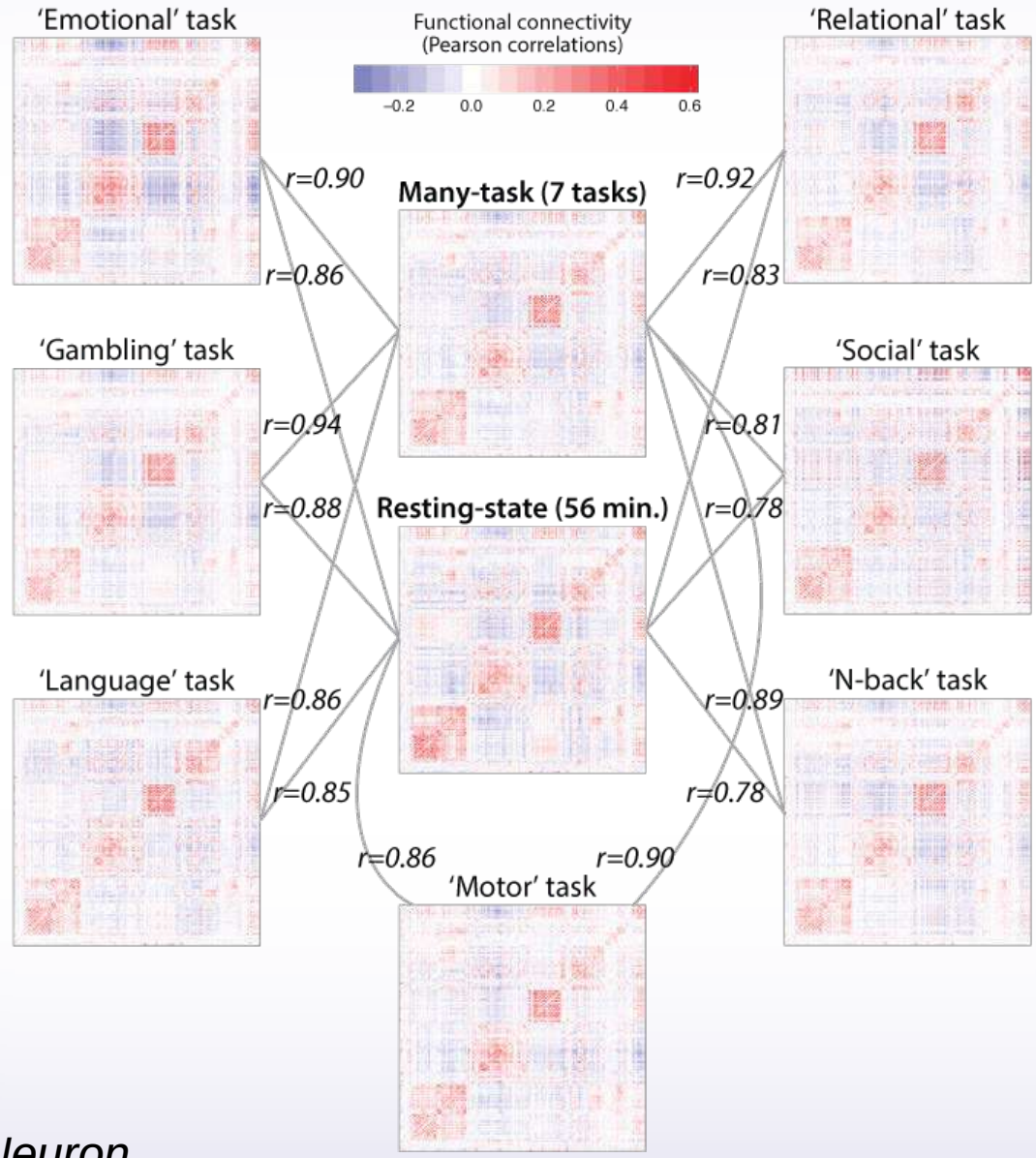
- Bifurcation into resting-state FC vs. task-evoked activation studies
- Rest FC patterns similar to task-evoked activation patterns
(Smith et al., 2009)
- But ***why***?
  - Need mechanism linking rest FC and activations





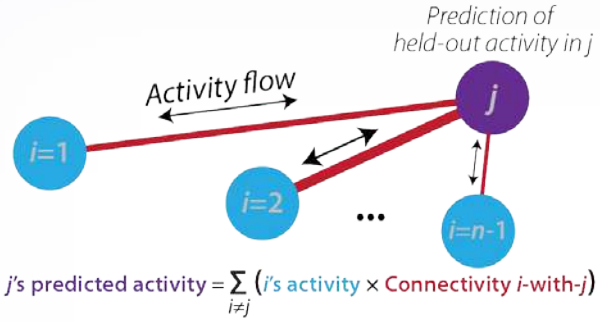


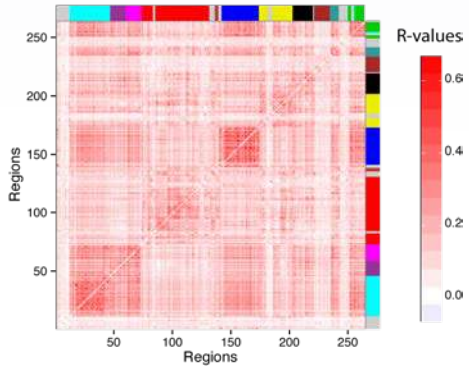
Highly similar FC patterns across mental states

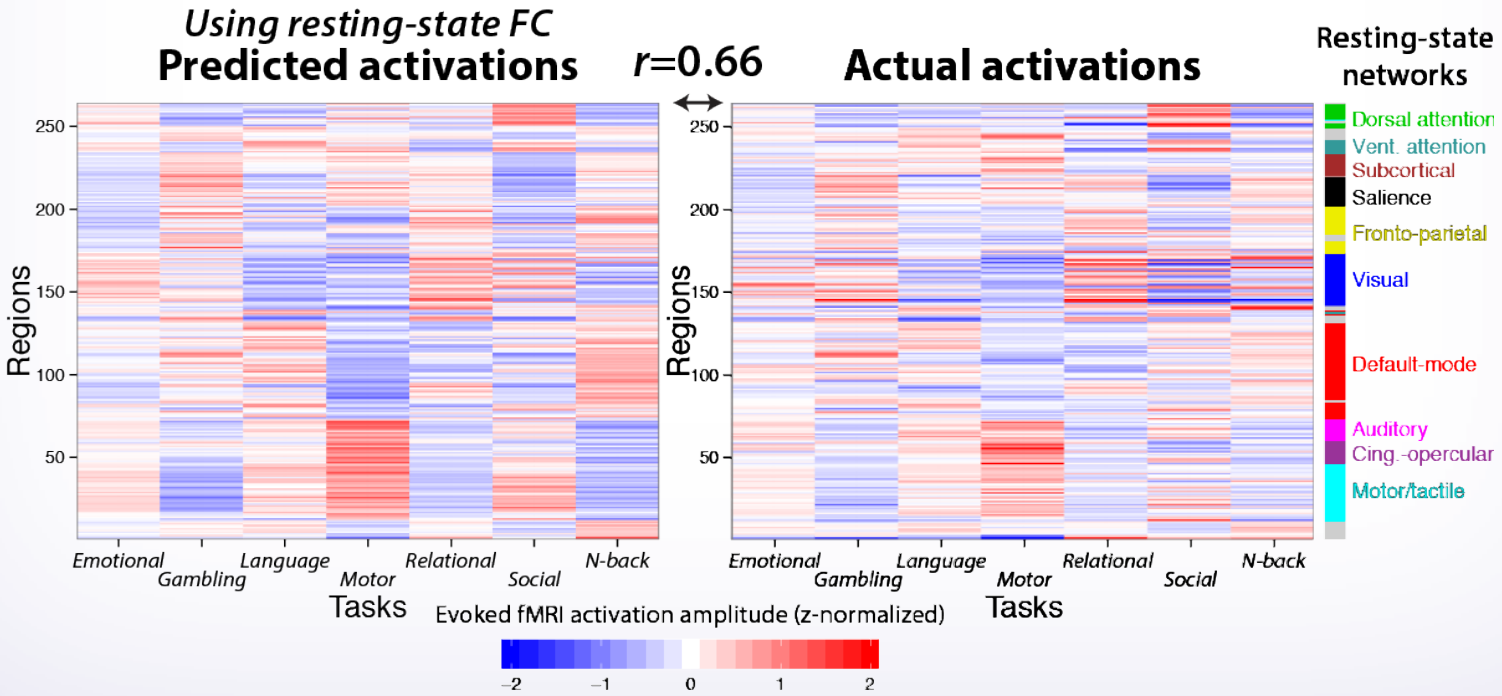


Cole et al., 2014; *Neuron*

Activity flow mapping

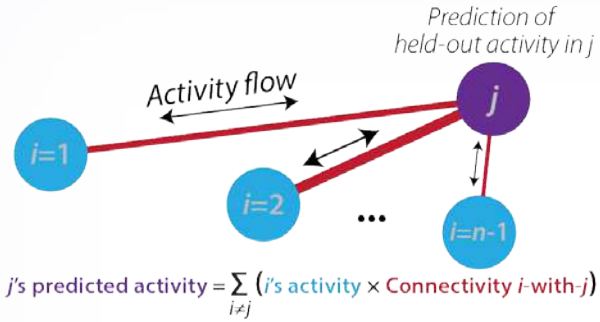


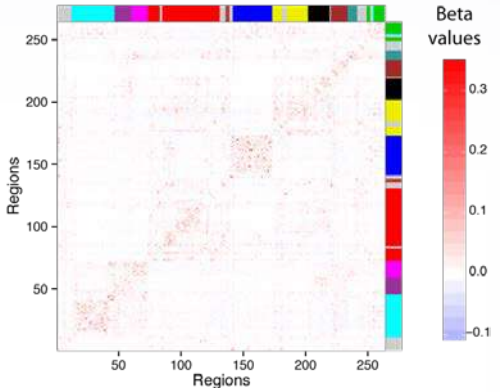


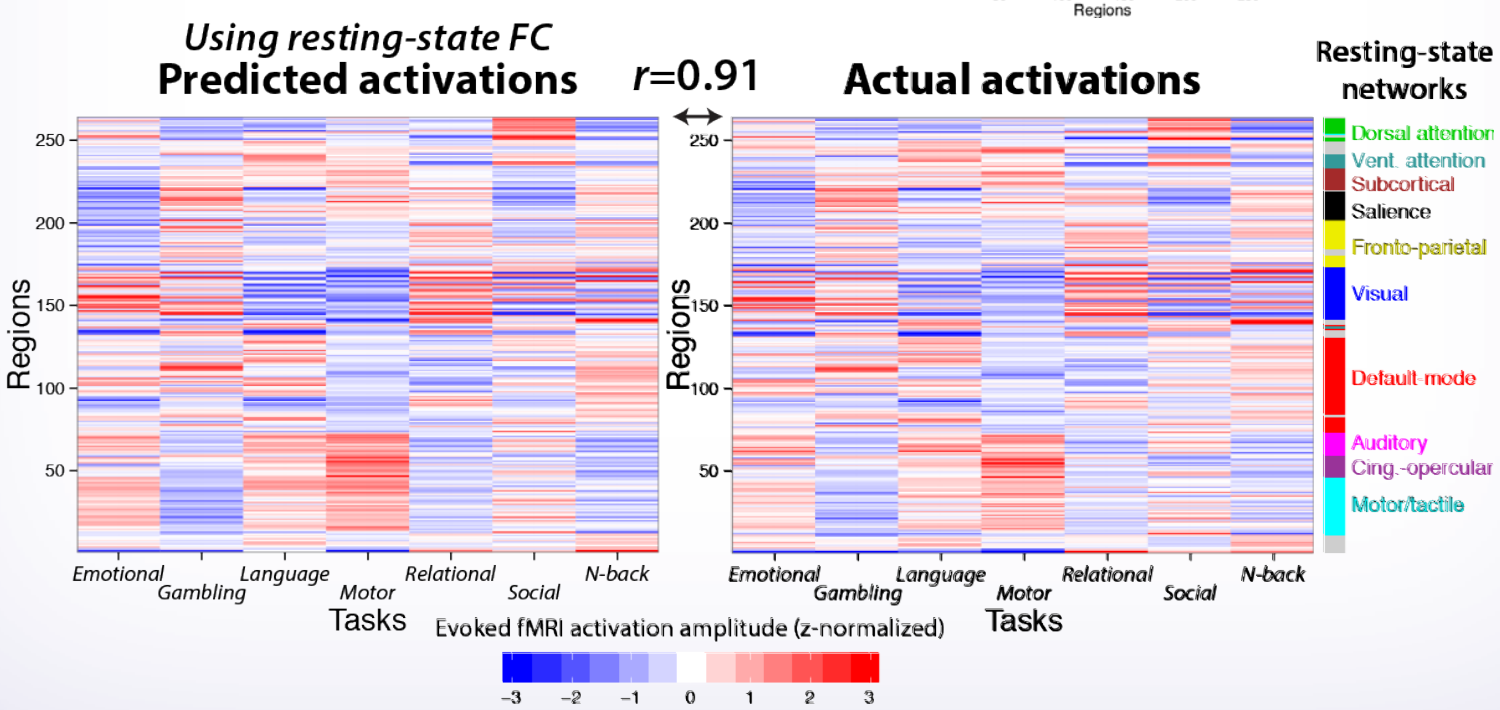


Cole et al., 2016; *Nature Neuroscience*

Activity flow mapping with multiple regression FC

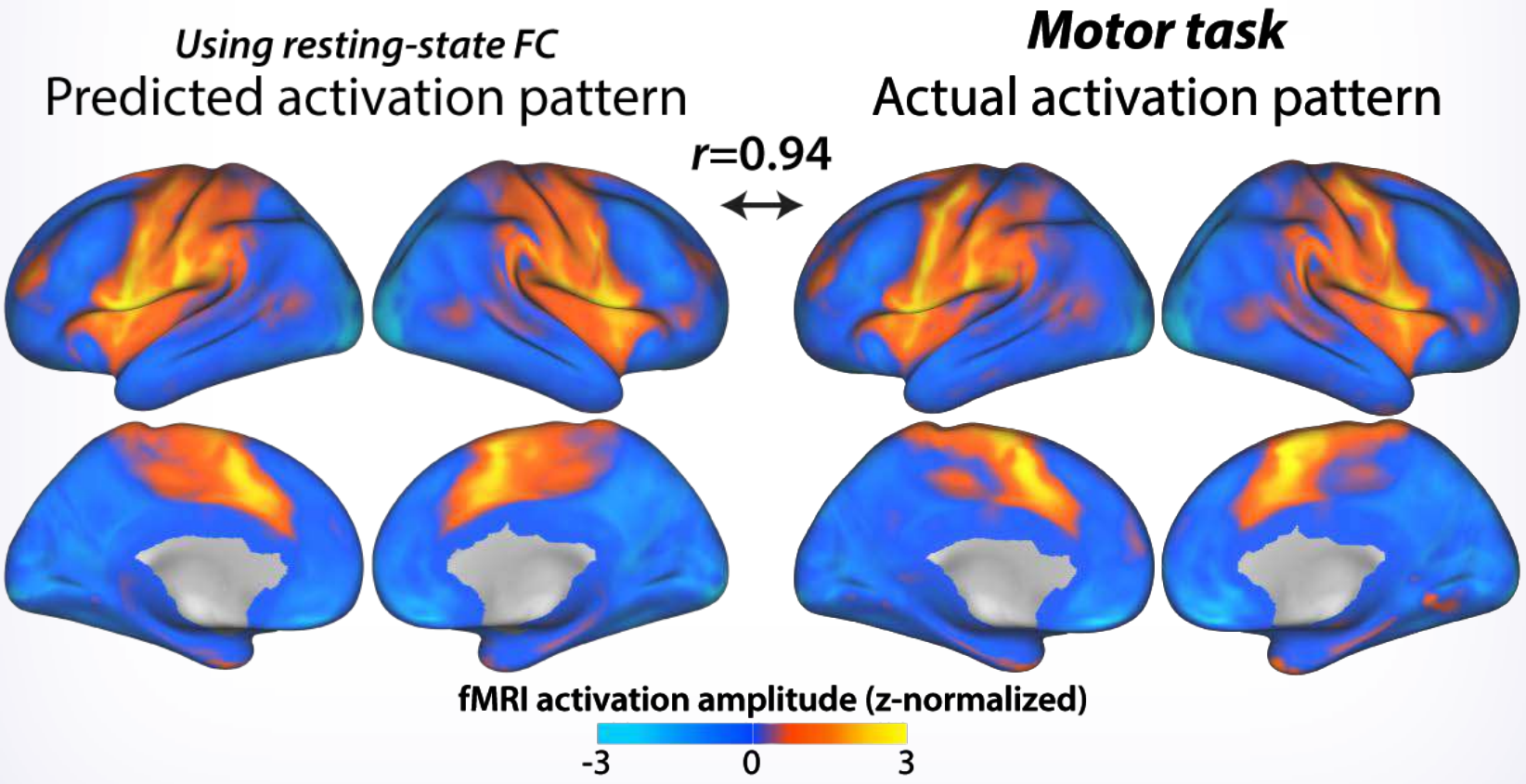






Cole et al., 2016; *Nature Neuroscience*

Activity flow mapping using multiple regression



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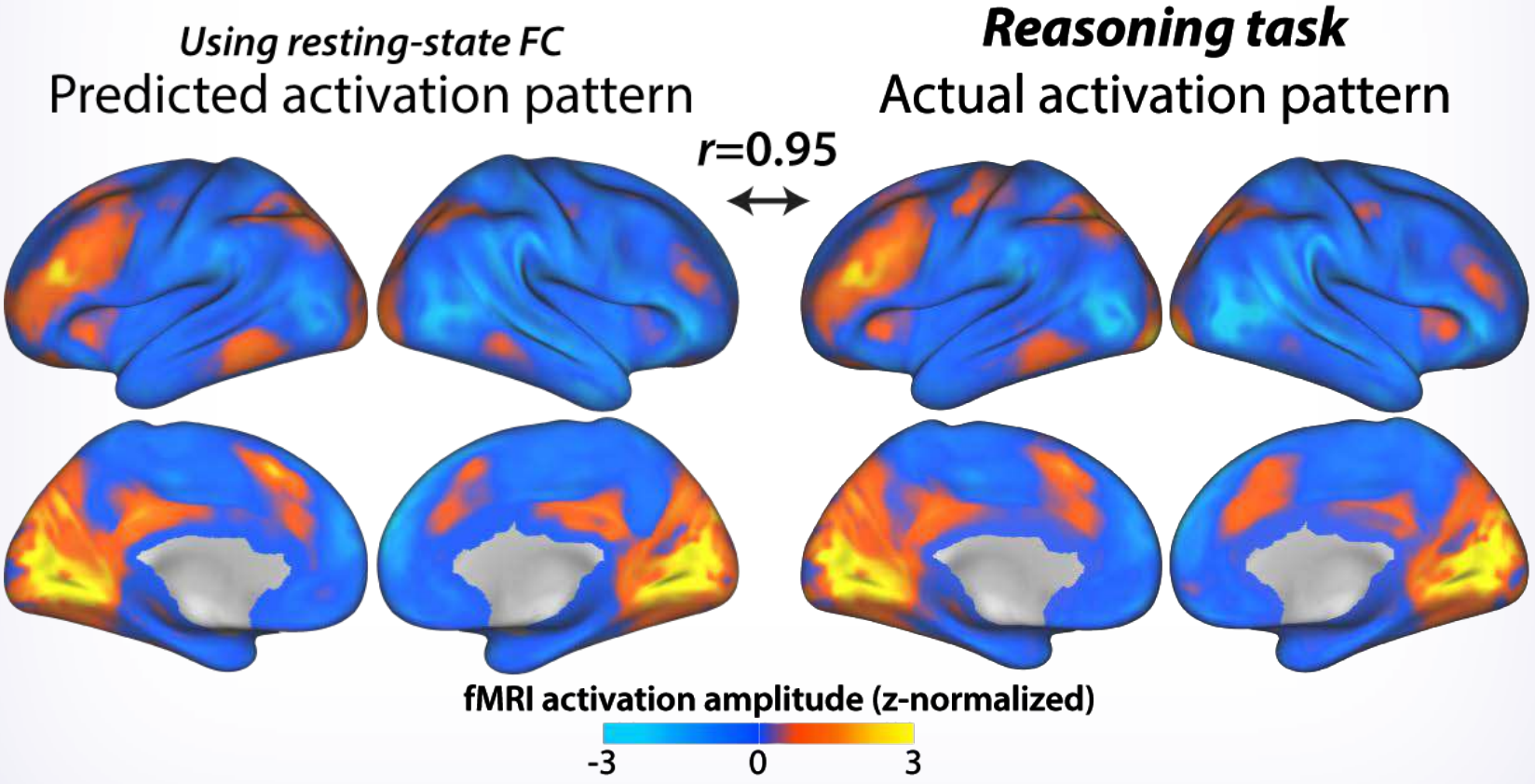

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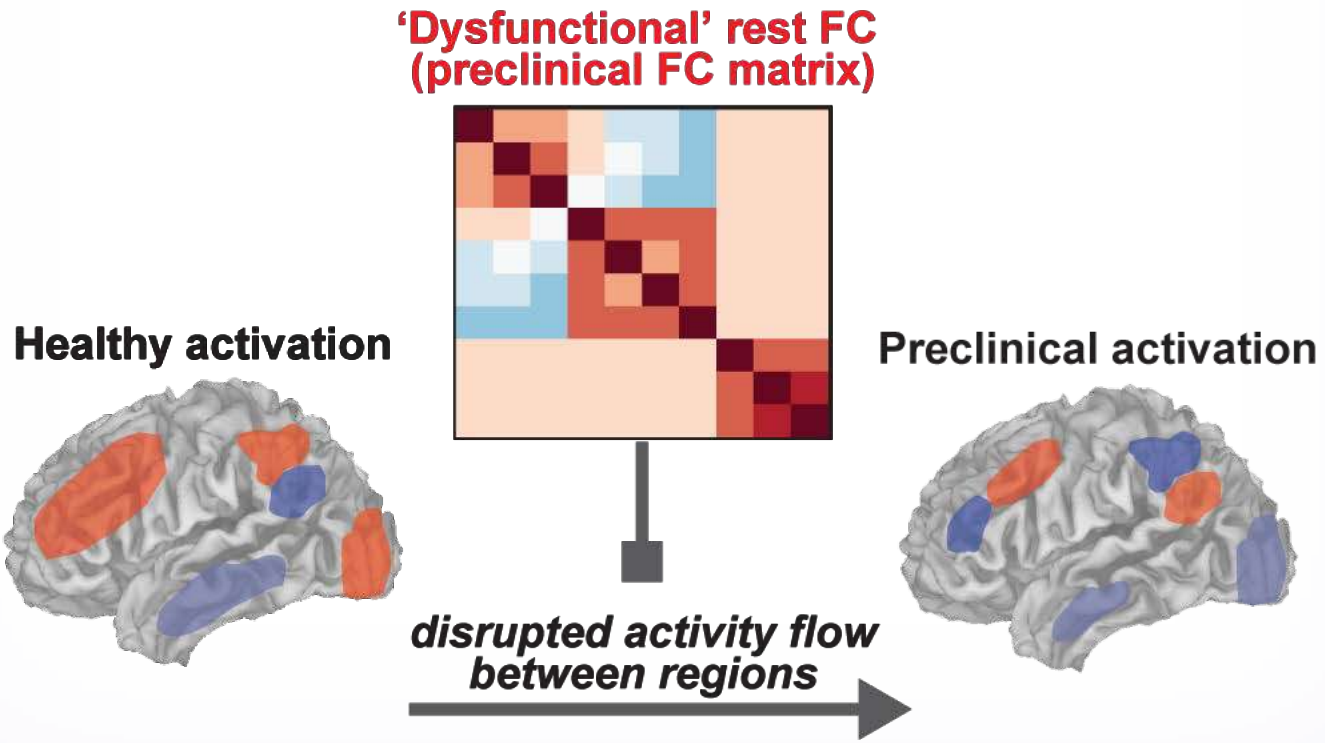
Predicting unhealthy aging-related cognitive activations

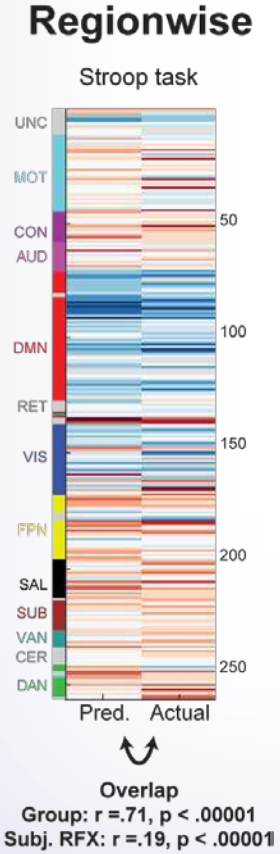


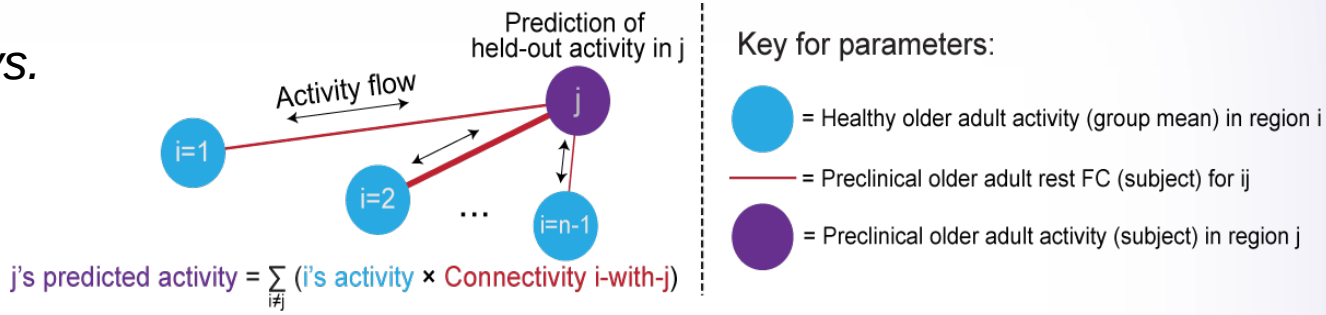
Subject characteristics: 101 cognitively-typical older adults, preclinical based on beta amyloid deposits or APOE genetic status

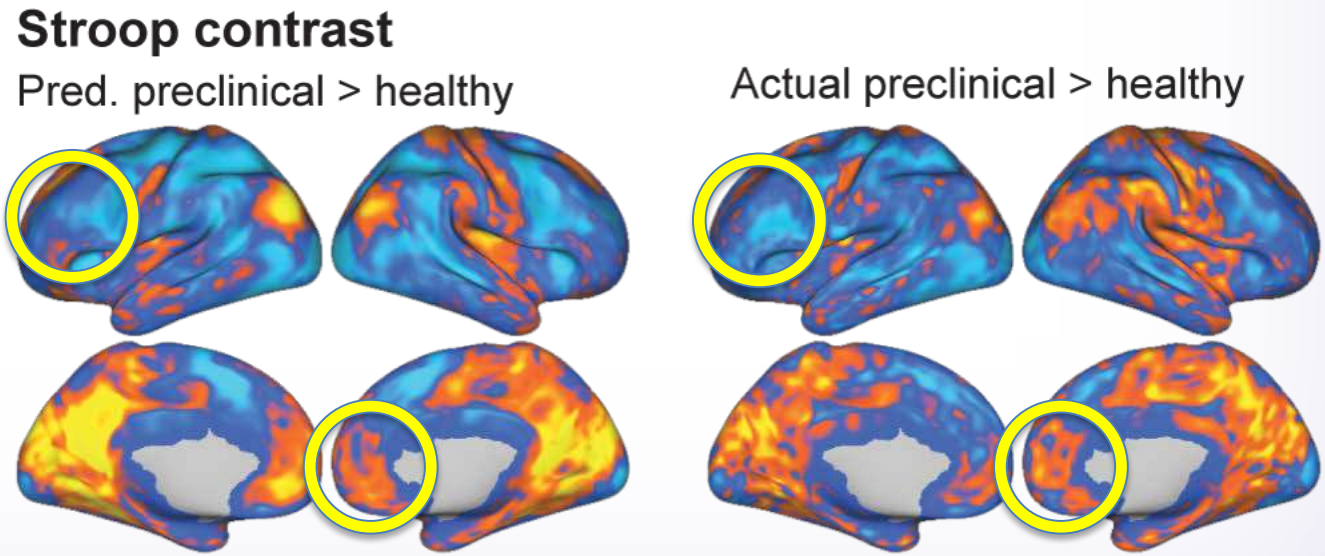
Mill et al., *in preparation*

Predicting unhealthy aging-related cognitive activations

Preclinical (APOE) vs. healthy older adults







Mill et al., *in preparation*

Take-home messages

- Large-scale FC provides insights into the neural mechanisms of cognition
- Activity flow mapping helps determine role of connectivity in cognitive task activations
  - Resting-state FC highly relevant to cognition
- Applied to aging research, activity flow provides insights & useful predictions

Integrative idea

- Rutgers-wide “big data” database for older adult recruitment and assessment
  - Include younger adults for matched aging controls, longitudinal studies (eventually they will be older!)
  - Healthy & unhealthy aging
  - State-wide practical: NJ most densely-populated state
- Study recruitment highly efficient, more valid
- *More studies possible*:
  Special subpopulations identifiable
- *More comprehensive assessment*:
  Pool data across studies for same individuals
- **Substantial advantage to Rutgers aging research**

Acknowledgements

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  - R01 from National Institute on Aging (NIA)

More information: **www.colelab.org**