Unveiling the cognitive relevance of functional connectivity through deconfounding

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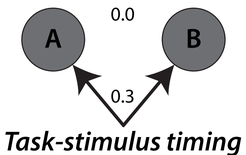
Task-stimulus confounding makes functional connectivity (FC) estimates less cognitively relevant

- Task-state FC estimates brain network changes during cognitive task performance
- Yet **task stimulus-evoked coactivations strongly confound FC estimation** (Cole et al., 2019), obscuring relationship between task-state FC and cognition
- Regularized partial correlation (Graphical Lasso, Glasso) reduces confounding for resting-state FC (Peterson et al., Preprint)
- ***Does Glasso also reduce task-stimulus FC confounding?***

No neural interaction

Observed correlation: 0.3
*Inference: "Likely interacting **or** active during task"*

Post-task-regression correlation: 0.0
Inference: "Unlikely to be interacting during task"

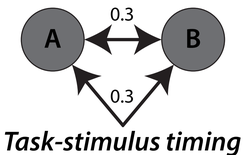


Task-stimulus timing

True neural interaction

Observed correlation: 0.6
*Inference: "Likely interacting **or** active during task"*

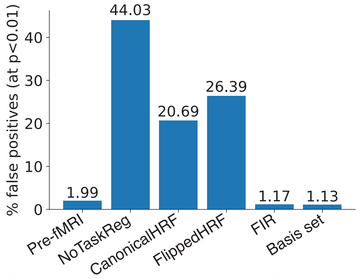
Post-task-regression correlation: 0.3
Inference: "Likely interacting during task"



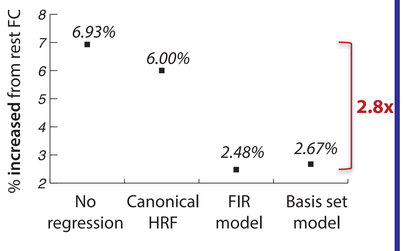
Task-stimulus timing

Standard approaches to reducing task-stimulus confounds are limited

Task-mean regression with *simulated* fMRI



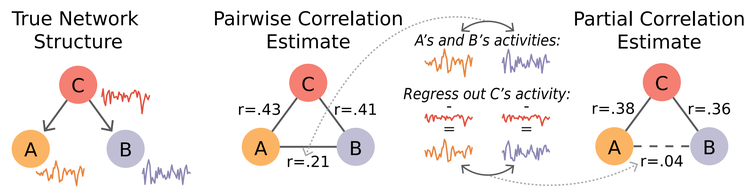
Task-mean regression with *empirical* fMRI data



- Regressing out mean fMRI activations prior to calculating task-evoked FC reduces false positives; accounting for variable HRF more effective – see **Cole et al. (2019)**
- Yet difficult to do & **still too many false positives** (threshold p<0.01)

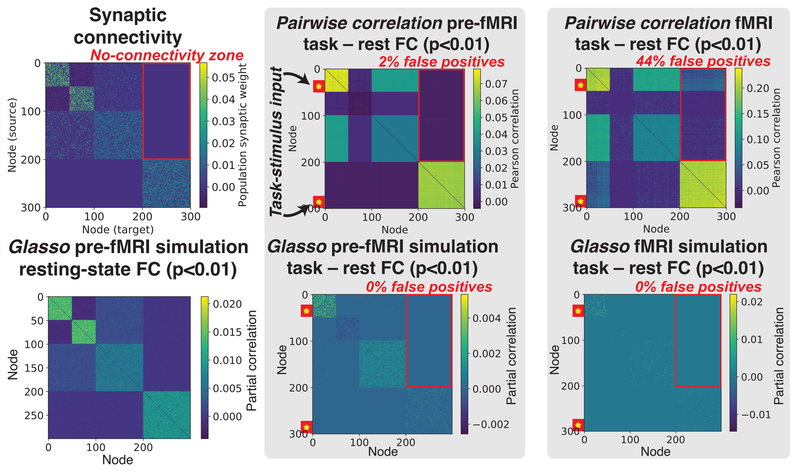
Regularized partial correlation (Glasso) for *general* FC confound reduction

Partial correlation estimates reduced-confound connectivity



- Partial correlation reduces false positives from confounds – see **Reid et al. (2019)**
- Regularization (e.g., Glasso) reduces false negatives, increases reliability – see **Peterson et al. (Preprint)**
- ***Does partial correlation reduce task-stimulus confounding?***

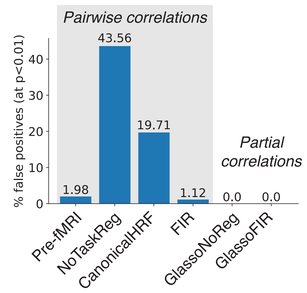
Simulations to test task-state FC confound reduction



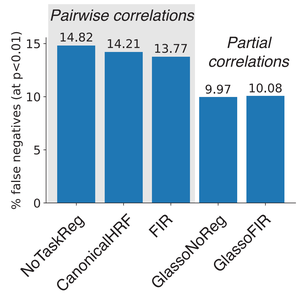
- Neural mass model, 300 nodes with 4 functional networks (see Cole et al., 2019)
- No-connectivity zone = no structural connections, no FC (direct or indirect)
- Pre-fMRI = neural simulation, fMRI = hemodynamic convolution added, downsampled
- Many false positives with Pearson correlation (2X pre-fMRI, 44X fMRI sims)
- ***False positives corrected by Glasso FC***

Regularized partial correlation (Glasso) reduces false positives & false negatives

False positives



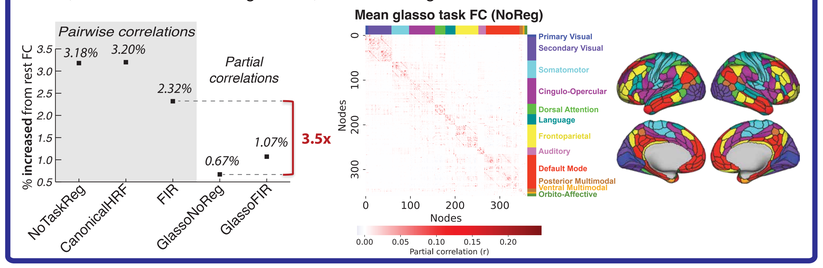
False negatives



- Glasso partial correlation reduced both false positives *and* false negatives
- False negatives defined relative to pre-fMRI (whole FC matrix)
- Adding FIR regression to Glasso FC did not improve FC estimation
- ***Regularized partial correlation improves task-state FC estimation***

Correcting task FC inflation in empirical fMRI data

- *Empirical fMRI data*: Human Connectome Project fMRI dataset (N=29), 7 tasks + rest, TR=720 ms, standard nuisance regression, removal of high-motion individuals



Summary & Conclusions

- **Does fMRI inflate task-state FC and can it be corrected?**
  Yes – FIR regression helps, but regularized partial correlation (e.g., Glasso) better corrects inflation and general confounding
- **Does partial correlation lead to false negatives?**
  No – Simulations show that false negatives decrease with Glasso

References: *Cole MW, et al. (2019). "Task activations produce spurious but systematic inflation of task functional connectivity estimates". NeuroImage.*
Peterson KL, et al. (Preprint). "Regularized partial correlation provides reliable functional connectivity estimates while correcting for widespread confounding". bioRxiv

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