Systematic differences between brain organisation revealed by task and rest

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Abstract

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Introduction

In neuroscience, the functional brain organization can be described brain parcellations, gradients or connectivity models. While each of these methods can be trained on either task-based or resting-state fMRI, resting-state has become the dominant approach due to its ease of acquisition and analysis. However, the brain is fundamentally an organ of behavior, and characterizing its organization during active cognitive states, like task performance, may offer more direct insights. While task-based approaches are well-suited for this, they impose a risk of biasing the fMRI responses to particular task sets. Multi-task fMRI paradigms offer a richer sampling of cognitive states and may therefore present a solution. Yet, multi-task and resting-state approaches have not been systematically compared in their ability to capture functional brain organization. This study presents a first systematic comparison of matched-duration resting-state and multi-task fMRI data across several preprocessing pipelines and validation metrics.

Methods and Results

We used 20 minutes of resting-state and task-based data each, acquired from the same seventeen subjects in the *Multi-Domain Task Battery* dataset (MDTB, King et al. (2019)). The multi-task data comprised 17 tasks tapping into cognitive, motor, perceptual, and social functions. During the resting-state session, subjects fixated on a fixation cross while letting their mind wander.

Data were preprocessed using SPM and Freesurfer with a minimal preprocessing pipeline including motion correction, registration to structural data, and cortical surface mapping. We then applied filtering steps commonly used in the field to compare their effects on the data (**Figure 1**). These were independent component analysis (ICA) based cleaning and connectivity fingerprinting. For connectivity fingerprinting, we used previously estimated connectivity weight maps (Nettekoven et al., 2024), consisting of 32 neocortical networks. We regressed the 32 group network spatial maps into each subject's data, to obtain subject-specific network time courses and calculated connectivity as the Pearson correlations of each voxel time series with each cortical network time course. For task data, we additionally calculated connectivity fingerprints on the residual time series after regressing out task-related fluctuations. Finally, we estimated beta maps using a general linear model (GLM) implemented in SPM12. Neocortical data was averaged within 1442 icosahedrons.

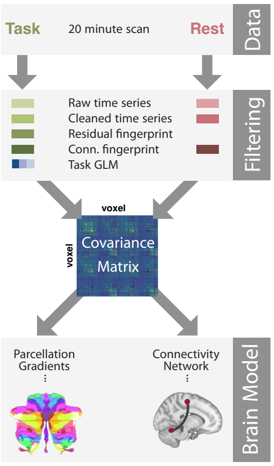

Figure 1: **Schematic of analysis pipeline.**

Most parcellation, gradient, or connectivity models depend only on the spatial covariance matrix, such that we can base our comparison of methods on this sufficient statistics of the data. We computed the parcel x parcel covariance matrix for each subject and each data type. We then quantified the reliability / similarity between two covariance matrices by calculating the Pearson correlation between their vectorized matrices.

Reliability

We first examined split-half reliability of the covariance matrices, estimated from two halves of the data (10 minutes scan time each). Although all data types showed some reliability (all $r > 0.55$, one-sample t-tests all $t_{16} > 11.67$, all Bonferroni-adjusted $p < 2.46 \times 10^{-8}$), we observed significant differences between the data types. Connectivity fingerprints calculated on task and rest data showed highest reliability followed by the cleaned task and rest time series. Task-related beta (mean activity) estimates showed lower split-half reliability, reflecting the dramatic data reduction when going from time series to activity estimates. Raw task and rest time series had lower reliability (task: 0.52 ± 0.22; rest: 0.55 ± 0.20).

Reliable covariance through measurement noise

While reliable data is necessary for capturing functional brain organization, it is not sufficient. In fact, high reliability of the covariance matrices can be due to measurement noise, such as motion or physiological artifacts. For example superior cerebellar voxels and the directly adjacent inferior occipital lobe often are correlated because they are physically close, even though they are separated by the tentorium and not functionally coupled (Buckner et al., 2011). While there is

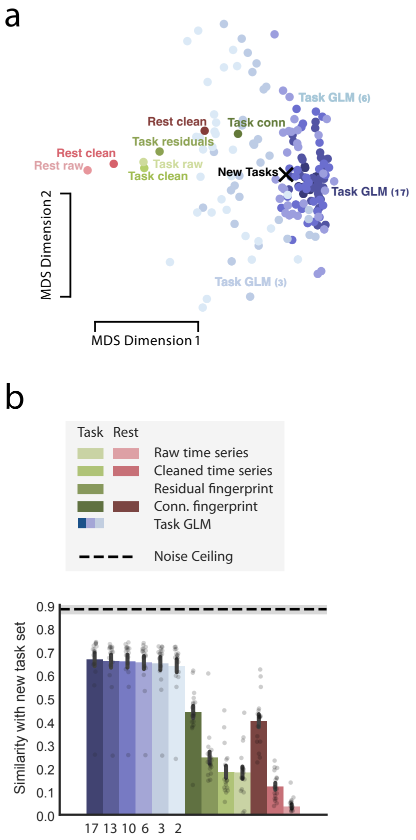

Figure 2: **Similarity space of covariance matrices**. **a** First two dimensions of the similarity space of covariance matrices. **b** Correlations of covariance matrices with the same individual's new task session.

no good general way to separate the covariance structure induced by measurement noise from those induced by neuronal processes, we can use the correlation of voxels across the tentorium as a rough proxy to gauge the degree to which different data types and processing pipelines are susceptible to these spurious correlations. We therefore calculated the normalized ratio between superior cerebellar and adjacent neocortical voxel correlations and superior cerebellar voxels and the rest of the neocortex as $\frac{r_{\text{non-adjacent}} - r_{\text{adjacent}}}{|r_{\text{non-adjacent}}| + |r_{\text{adjacent}}|}$. Because we would expect that spatial adjacent correlations mostly reflect measurement noise correlations, we expected better methods to have more positive values. As a ground-truth estimate, we also estimated the metric using cross-validation, where the neocortical and cerebellar beta estimates were acquired in different runs. As expected, we found positive coefficients for the crossed betas (mean: 0.60 ± 0.46, one-sample t-test against 0: $t_{16} = 5.47$, $p = 5.16 \times 10^{-5}$). Next, we calculated internal validity for data from the same runs. We found that task betas showed the highest coefficients, exceeding all other data types (mean 0.147 ± 0.142, all $t_{16} > 3.47$, all Bonferroni-adjusted $p < 2.52 \times 10^{-2}$). This confirmed that despite its relatively low split-half reliability, task betas were least influenced by proximal noise correlations.

Similarity of task sets to each other

A common concern with using a task-based approach is that the resulting activity will be biased by the specific task set. We hypothesized that any bias towards a particular task state should reduce with the inclusion of more tasks. We randomly sampled task batteries of 2, 3, 6, 10 and 13 tasks from 17 possible tasks, with 20 minutes scan time each. We then correlated the resulting covariance matrices with all other covariance matrices of the same task battery size. As hypothesized, we found that the similarity between task batteries increased with task battery size, with similarity plateauing at 10 tasks sampled (significant difference of 10 tasks to 6, 3, 2 tasks: all $t_{16} > 2.91$, $p < 1.02 \times 10^{-2}$, but no significant difference to 13 or 17 tasks: all $t_{16} < 0.30$, $p > 0.76$). The influence of the specific task set therefore reduced with the number of tasks.

Generalization to novel task set

A good estimate of functional organization should generalize to a wide variety of brain states. We therefore evaluated the ability of the covariance matrices derived from different data types in predicting functional organization in a separate task session of 9 new tasks with 144 minutes scan time. Again, we calculated similarity as the Pearson correlation of the vectorized covariance matrices. A multi-dimensional scaling plot shows the first two dimensions of the similarity space of the covariance matrices (**Figure 2a**). We observed that filtering the data reduced the distance to the new tasks: cleaned time series data showed higher similarity with the evaluation task set than raw time series data numerically. Connectivity fingerprinted data showed significantly higher similarity than cleaned time series data (rest: $t_{16} = -7.89$, $p = 6.65 \times 10^{-7}$; task: $t_{16} = -11.02$, $p = 7.03 \times 10^{-9}$). Task data consistently captured functional organization better than rest data (rest vs. task data types: all $t_{16} < -2.53$, all Bonferroni-adjusted $p < 2.21 \times 10^{-2}$). Finally, task betas captured functional organization in the evaluation task set best, showing highest similarity to the new tasks (all $t_{16} > 3.73$, all Bonferroni-adjusted $p < 2.38 \times 10^{-2}$).

Discussion

We here show that the data modality (resting-state or task-based) and filtering choices strongly influences the structure of the estimated covariance matrix. While covariance matrices estimated from time series data are very reliable, they are also biased by measurement noise, leading to a systematic deviation from the covariance structure estimated from a broad task battery. Covariance structures estimated from task-related activation maps depend highly on the specific task, a problem that is mitigated when including more tasks. Finally, we find that task betas show a substantial advantage in predicting functional organization in a separate deep phenotyping session of unobserved task states.

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References

Buckner, R. L., Krienen, F. M., Castellanos, A., Diaz, J. C., & Thomas Yeo, B. T. (2011). The organization of the human cerebellum estimated by intrinsic functional connectivity. *Journal of Neurophysiology*, *106*(5), 2322–2345. doi: 10.1152/jn.00339.2011

King, M., Hernandez-Castillo, C. R., Poldrack, R. A., Ivry, R. B., & Diedrichsen, J. (2019). Functional boundaries in the human cerebellum revealed by a multi-domain task battery. *Nature Neuroscience*, *22*(8), 1371–1378. doi: 10.1038/s41593-019-0436-x

Nettekoven, C., Zhi, D., Shahshahani, L., Pinho, A. L., Saadon-Grosman, N., Buckner, R. L., & Diedrichsen, J. (2024, sep). A hierarchical atlas of the human cerebellum for functional precision mapping. *Nature Communications*, *15*(1), 8376.