Physiological Signatures Across the Brain

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HIGHLIGHTS

Physiological variance in BOLD signals may:

- correspond to unique properties of individual subjects.
- carry information about behavioral and cognitive traits.
- provide insights into the complex interplay between brain function, individual differences, and behavioral outcomes.

INTRODUCTION

Background: Fluctuations in low-frequency systemic physiology (e.g., respiration and cardiac activity) are often treated as nuisance components in fMRI research.

Motivation: However, an increasing number of studies indicate that they contain meaningful untapped information about brain physiology and autonomic function [1,2,3,4].

Gap: Yet, the potential heritability and behavioral relevance of systemic, low-frequency BOLD effects, and their large- scale patterns across the brain, are largely underexplored.

Aim: Systematically examine patterns of peripheral physiological influences in fMRI signals and their association to individual differences in behavior.

METHODS

Dataset: A subset of 375 subjects from the HCP S1200 release was utilized based on the quality of their physiological recordings [5,6]. Dataset included:

- resting-state data (4 scans/subject, 2 days with 2 runs on each day)
- 51 cognitive measures based on the exclusion criteria from [7] and their availability in the HCP "unrestricted" behavioral assessments.

Data Prep: The percentage of temporal variance accounted for by respiratory volume (RV) and heart rate (HR) regressors convolved with respiratory and cardiac response function basis sets [8,9] was calculated at each fMRI voxel. The percent variance explained (PVE) maps were deconfounded for sex, height, weight, intracranial volume, brain size, and average movement in scanner.

Similarity Analysis: To assess the stability of physiological signal patterns, we employed a correlation analysis. For both within-day and between-days scans of a given subject, percent variance maps were compared using voxelwise Pearson correlation. Significance testing was performed with a 5000-iteration permutation test, wherein the physiological data were randomly shuffled across all subjects.

Heritability Analysis: First, we assess the spatial similarity of BOLD physiological patterns among family members and other subjects. Next, we use SOLAR-Eclipse imaging genetic analysis package [10] to quantify this similarity. Phenotype values for each individual within the cohort were adjusted for covariates including sex, age, age2, age × sex interaction, age2 × sex interaction, height, weight, intracranial volume, brain size, and average movement in scanner.

Canonical Correlation Analysis: To investigate a linear association between BOLD physiological patterns and behavioral/cognitive variables, we employed CCA. Prior to CCA dimensionality reduction of both brain and behavior data was carried out using PCA with 30 brain and 2 behavioral PCs (a sensitivity analysis was performed on the number of PCs, not shown).

RESULTS

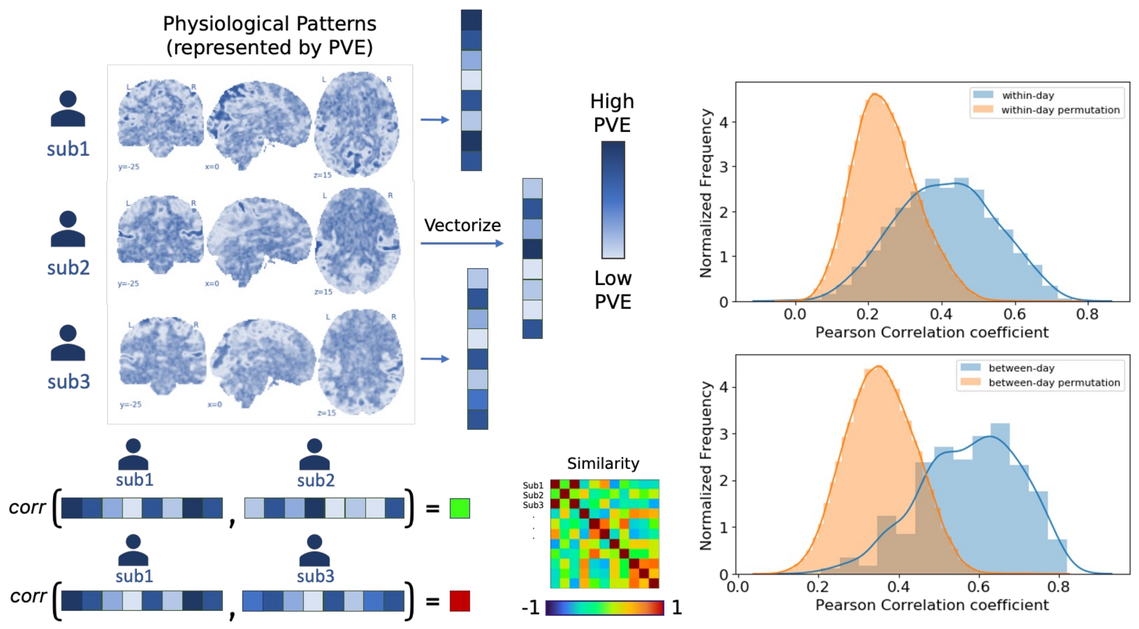

Fig. 1 (left) Illustration of similarity assessment between percent variance explained (PVE) maps across subjects. (right) Intra-subject similarity assessment within and between days. Within-day and between-day similarity is showcased to examine the consistency of BOLD physiological patterns for each subject over time. Histograms marked with blue color demonstrate the comparison of these patterns, providing insights into the stability of observed patterns across different scans. Histograms marked with orange color depict a null distribution resulting from randomizing the data distribution.

RESULTS Cont'd

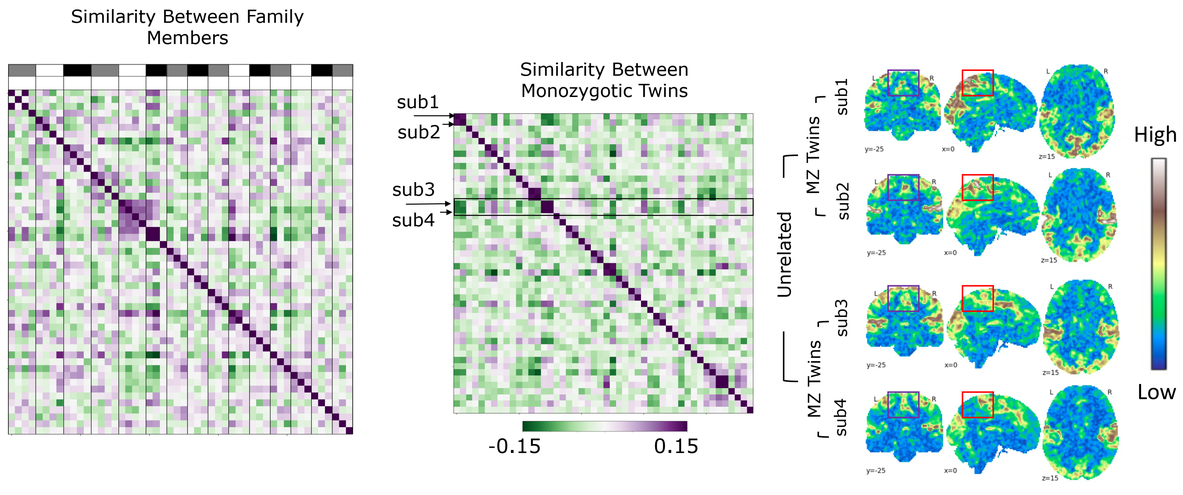

Fig. 2 Family-structured physiological patterns. (left and middle) The similarity matrices visually represent the relationship between BOLD physiological patterns among family members and other subjects. Each row and column in the matrix corresponds to an individual participant, where family members are grouped together. The matrix is color-coded to reflect the degree of similarity, with purple hues indicating higher similarity and green hues indicating lower similarity. By examining the matrix, we gain insights into the shared physiological patterns within families and their distinctiveness compared to patterns observed in other subjects. (right) The twin samples of PVE maps illustrate the relationship within and between twins. Monozygotic (MZ) twins exhibit stronger correlations within the same family and exhibit distinct spatial variations compared to the two sets of other twins.

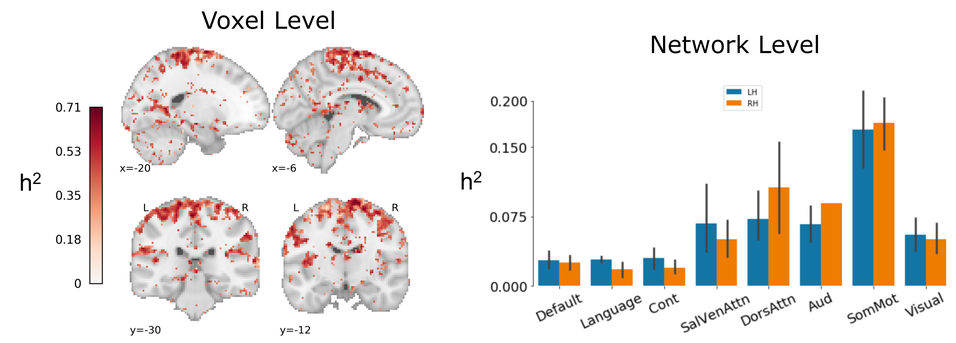

Fig. 3 Heritability (h^2) is computed using SOLAR-eclipse. h^2 is the proportion of the total phenotypic variance that can be explained by the genetic effects. (left) Voxel level maps indicating the h^2, thresholded at a $p<0.05$ uncorrected threshold. (B) Network-level averages of h^2, shown for left and right hemispheres.

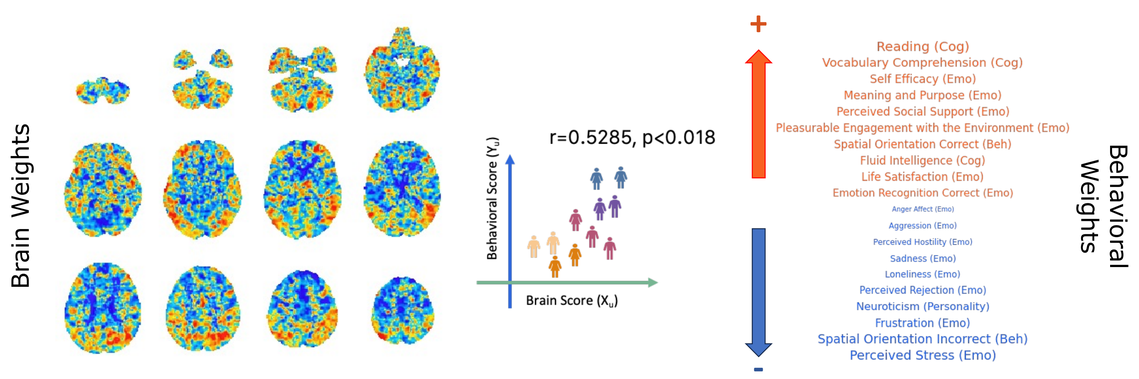

Fig. 4 CCA yielded a significant first canonical mode between the physiological patterns and the phenotypic profiles of the population ($p<0.018$). (left) The first canonical mode and its maps of the brain CCA weights, and (right) the top 10 positive and negative CCA behavioral weights. Notably, this mode combines positive weights associated with both cognitive traits and positive emotional attributes, indicating a positive relationship between these traits and this brain mode. Conversely, negative weights were primarily observed in more negative self-report measures.

CONCLUSIONS

- In this study, we explored the potential of BOLD physiological signatures to serve as predictors of cognitive and behavioral variables.
- The variability observed in physiological signals captured by BOLD signals may reflect unique characteristics of individual subjects.
- By considering and analyzing these measures, we gain valuable insights into the complex interplay between brain function, individual differences, and behavioral outcomes.
- Heritability analysis provides valuable information on the potential influence of genetic and environmental factors on the observed spatial physiological patterns.
- Physiological signals are closely linked to brain function and have connections to behavior. Removal of these signals should therefore depend on the study.

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NEURDY lab git repo for code and more: github.com/neurdylab

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