

# Predicting psychometric data from functional connectivity in healthy adults: progress and pitfalls

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Symposium

In this symposium, we will first present general guidelines pertaining to the use of supervised machine learning models for predicting psychometric data that have been recently proposed. We will next present recent findings on the influence of the denoising approaches of RSFC on the prediction performance. We will then examine the question of whether connectomic predictive methods can inform models of how psychometric constructs are interrelated, focusing on a longstanding debate in psychology about the architecture of cognitive abilities. Finally, we will present a recently proposed region-based prediction framework aiming to examine the biological validity and, hence, the interpretability of such machine learning approaches in a cognitive neuroscience perspective.

## Objective

Having taken part in this symposium, participants should better understand

- 1) how to design predictive models of psychometric variables based on resting-state functional connectivity.
- 2) The participants should also be more aware of the limitations of approaches aiming to relate psychometric data to brain features in healthy populations,
- 3) as well as the influence of confounding variables and noise in these approaches.

## Target Audience

The human brain mapping community. This symposium combines methodological and crucial conceptual aspects and will be of interest for researchers in the field of functional connectivity, brain-behaviour mapping, as well as cognitive and clinical neuroscientists interested in the potential applications and interpretation.

## Presentations

### Simple guidelines for predictive modeling (and when to break them)

Establishing brain-behavior associations that map brain organization to phenotypic measures and generalize to

novel individuals remains a challenge in neuroimaging. Predictive modeling approaches that define and validate models with independent datasets offer a solution to this problem. While these methods can detect novel and generalizable brain-behavior associations, they can be daunting, which has limited their use by the wider connectivity community. Here, we offer some simple guidelines implementing these approaches. However, as all good rules are meant to be broken, we will highlight a few special cases where deviations from these guidelines may offer preferred solutions to the neuroimaging community.

### Presenter

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## **Global Signal Regression Strengthens Association between Resting-State Functional Connectivity and Behavior**

Global signal regression (GSR) is a controversial but widely used preprocessing step in studies of resting-state functional MRI (rs-fMRI) of human brain activity, due to the complex mixture of noise and neural information in global signal. Given significant interest in the relationship between human behavior and functional brain architecture revealed by rs-fMRI, this presentation will focus on the utilitarian question of whether GSR strengthens or weakens associations between resting-state functional connectivity (RSFC) and multiple behavioral measures across cognition, personality and emotion. Two large-scale datasets were utilized: (a) the Brain Genomics Superstruct Project (GSP), N = 862, 23 behaviors; (b) the Human Connectome Project (HCP), N = 953, 58 behaviors. By applying the variance component model, we found that behavioural variance explained by whole-brain RSFC increased by an average of 40-50% in the two datasets respectively. To ensure generalizability, we repeated our analyses using kernel regression. GSR improved behavioral prediction accuracies by an average of 64% and 12% in the GSP and HCP datasets respectively. Importantly, the results were consistent across methods. A behavioral measure with greater RSFC-explained variance (using the variance component model) also exhibited greater prediction accuracy (using kernel regression). A behavioral measure with greater improvement in behavioral variance explained after GSR (using the variance component model) also enjoyed greater improvement in prediction accuracy after GSR (using kernel regression). Furthermore, GSR appeared to benefit task performance measures more than self-reported measures. Overall, our results suggest that at least in the case for young healthy adults, GSR strengthens the associations between RSFC and most (although not all) behavioral measures.

### Presenter

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## **Can Connectomics Clarify the Architecture of Cognitive Abilities?**

The architecture of cognitive abilities has been one of the most hotly contested topics in the history of psychology. According to strong versions of “g theory”, there is a single unified brain basis for performance across diverse cognitive tasks (Spearman, Jensen). At the opposite extreme, some theorists claim psychometric g is nothing more than a statistical artifact and there is nothing in our brain to which it corresponds (Gould, Conway). Recent years have seen the rise of predictive modeling methods that identify distributed connectomic signatures associated with performance on cognitive tasks. These new developments raise the question of whether connectomic

methods can inform longstanding debates about the architecture of cognitive abilities. For example, if connectomic signatures of task performance are highly similar across diverse cognitive tasks, this suggests these tasks share a common connectomic basis. On the other hand, if they are very dissimilar, this counts as evidence against g theory. To address this question, we introduce response network correspondence analysis (RNCA). We start with a set of cognitive tasks for which there are moderate intercorrelations in behavioral performance. We next construct a response network for each task (e.g., a connectomic signature of task performance). Because the tasks are behaviorally correlated, the response networks will necessarily be similar. RNCA uses non-parametric permutation methods to answer the question of whether the observed similarity in response networks is greater than one should expect by chance, indicating there is a common underlying connectomic basis across tasks. We applied RNCA to two large resting state fMRI datasets: the Human Connectome Project (n=910; 10 cognitive tasks) and the Adolescent Brain Cognitive Development dataset (n=2013; 11 cognitive tasks). In both datasets, we performed bifactor modeling on behavioral data and constructed a general factor of cognitive ability (“g factor”). Results from RNCA conducted at both the whole brain level as well as with 78 network pairs (involving 13 networks) showed no statistically significant results. That is, we found no evidence that response networks are shared across cognitive tasks above chance levels. We supplemented RNCA with two additional analyses. The first examined the count of connections maximally correlated with g (as opposed to being maximally correlated with an individual cognitive task). The second examined the count of connections that are correlated above some threshold value with performance on multiple individual cognitive tasks (allowing us to ask whether there are “multiple demand” edges that tend to support performance across numerous, i.e., > 4, tasks). In both analyses, these counts were no higher than one should expect by chance. Taken together, our analyses find no evidence for a shared connectomic basis for performance across diverse cognitive tasks that is predicted by g theory.

## Presenter

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## **A Connectivity-based Psychometric Prediction Framework for Brain-behavior Relationship Studies**

Evident from the other presentations, the recent availability of population-based studies with standard neuroimaging measurements and extensive psychometric characterization has enabled many investigations about the relationships between interindividual variability in brain regions’ connectivity and behavioral phenotypes. However, the multivariate nature of prediction models based on connectivity within a network of brain regions severely limits the interpretation of the brain-behavior patterns from a cognitive neuroscience perspective. To address this issue, we here propose a connectivity-based psychometric prediction (CBPP) framework based on individual region’s connectivity profile. Preliminary to the development of this region-wise machine learning approach, we performed an extensive assessment of the general CBPP framework based on whole-brain connectivity information. Because a systematic evaluation of different parameters was lacking from previous literature, we evaluated several approaches pertaining to the different steps of a CBPP study. We hence tested 72 different approach combinations on the Human Connectome Project (HCP), in a cohort of over 900 healthy adults across 98 psychometric variables. Using optimal approaches based on whole-brain CBPP, we then implemented parcel-wise CBPP, where we evaluated a prediction model from each brain region/parcel independently. To promote the use of this framework in cognitive neuroscience studies, we illustrated two main applications: 1) single brain region’s predictive power for different psychometric variables 2) variation of predictive power across brain regions for a single psychometric variable. Overall, our extensive evaluation combined to an innovative region-wise machine learning approach, offer a framework that optimizes both prediction performance and

neurobiological validity (and hence interpretability) to study brain-behavior relationships.

## Presenter

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