# Prediction-Identification Landscape for Brain Structure and Connectivity

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## Synopsis

**Neuroimaging-derived brain phenotypes can be used to identify individuals and predict behavior. We investigated the prediction and identification performance of brain structure and connectivity phenotypes derived from structural, functional and diffusion MRI. Five behavioral domains were predicted: cognition, illicit substance use, tobacco use, personality-emotion traits, and mental health. We arranged the phenotypes on a two-dimensional prediction-identification landscape. Functional connectivity performed better at prediction than identification, whereas the converse was found for curvature and other structural phenotypes. Structural connectivity performed well for both tasks. High-resolution measures outperformed atlas-based counterparts. Our work can aid brain phenotype selection in future neuroimaging studies.**

## Introduction

Multimodal neuroimaging provides the ability to noninvasively measure brain phenotypes such as cortical architecture, topography, function, and connectivity. A major goal in neuroscience is to establish whether these phenotypes predict individual variation in human behaviors and cognitive performance[1,2,3]. We refer to this as *behavior prediction*. Functional connectivity (FC) is known to predict individual variation in fluid intelligence[4], sustained attention[5], and a myriad of other behaviors[6]. In contrast, fewer studies have investigated behavior prediction with structural connectivity (SC) derived from diffusion MRI[7].

A complementary and more recently investigated goal involves determining whether neuroimaging-derived phenotypes can identify specific individuals from a group of others, which is referred to as *individual identification*, otherwise known as *neural fingerprinting*[4]. Individual variability in FC is sufficiently large[3] to enable individual identification based on an individual's unique FC fingerprint[4,8,9,10]. However, it is unclear whether SC fingerprints[11] or alternative neuroimaging-derived measures are more unique to individuals than FC and thus would enable improved individual identification.

The aim of this study was to compare the identification and behavior prediction performance of neuroimaging-derived phenotypes, including FC, SC and various measures of cortical structure and architecture. We also investigate whether high-resolution connectomes and cortical structure measured at the resolution of vertices/voxels provide improved identification and prediction performance, compared to their atlas-based counterparts. Figure 1 shows an overview of the study design and summarizes the key neuroimaging phenotypes investigated.

## Methods

We analyzed neuroimaging and behavioral data acquired from 1000 individuals participating in the Human Connectome Project (HCP)[12]. These individuals formed a *test* group. MRI scans were repeated in 42 of these individuals, providing a *retest* group. Diffusion MRI and probabilistic tractography was used to map structural connectomes. Functional connectomes were mapped using resting-state functional MRI. Connectomes were mapped at the resolution of cortical surface vertices (~32,000 nodes per hemisphere) and regions comprising an established atlas (180 nodes per hemisphere)[13]. Additionally, cortical surface maps of: i) cortical thickness, ii) cortical curvature, iii) sulcal depth, and iv) myelin were sourced from the HCP. These maps were also resampled to the atlas regions. Hence, each individual was associated with two connectomes and four surface maps, each of which was mapped at the resolution of vertices and regions, yielding 12 measures in total. For each measure, a similarity metric for all test-test ($1000 \times 1000$) and test-retest ($1000 \times 42$) pairs of scans was computed.

***Individual Identification:*** Each fingerprint in the retest group was matched to the fingerprint in the test group with which it was most similar. This is yielded a one-to-one mapping between individuals in the retest and test groups. The fingerprint-predicted matching was compared to the ground truth to determine the proportion of correctly matched individuals in the retest group, referred to as the identification accuracy. Given that multiple phenotypes yielded $100\%$ accuracy, identification performance was also measured using the effect size difference (Cohen's d) between the distribution of i) true pair similarities ($42$ pairs), and ii) false pair similarities ($42 \times 999$ pairs). Hence, higher effect size differences translated to higher precision in identification.

***Behavior Prediction:*** Independent component analysis (ICA) was used to decompose 109 behavioral measures[14] to five core continuous dimensions, characterizing cognitive performance, illicit substance use, tobacco use, personality-emotion traits, and mental health. Fluid intelligence was also considered to facilitate comparison with existing studies. The variance component model (VCM)[15] was used to evaluate the extent to which each neuroimaging measure could explain individual variation in each behavioral dimension. Measures that explained greater individual variance were deemed to perform better. The similarity matrix for the VCM was computed by correlating each measure between pairs of individuals.

## Results

***Individual Identification:*** We found that measures of cortical structure and architecture, such as curvature, are more accurate in fingerprinting individuals than functional connectivity (Figure 2:A). Crucially, fingerprints derived from structural connectivity enabled the most accurate identification of individuals. Additionally, the vertex-based variants that were computed in higher resolution generally improved identification performance to a great extent.

***Behavior Prediction:*** For behavior prediction, Figure 2:B shows the variance explained in VCM averaged across the independent components of cognition and behavior sampled with a jackknife resampling method[16]. This can be interpreted as an overall rating of the applicability of neural phenotypes to a wide range of cognitive and behavioral characteristics. We found that connectomic measures in general, especially at the higher resolution, better explained individual variation in behavior. (See Figure 3 for a detailed breakdown of behavior interpretation components.) A measure of individual uniqueness was also computed by regressing out the false pair similarities from the true pair similarities (Figure 4).

## Discussion and Conclusion

Arranging neuroimaging-derived phenotypes on a two-dimensional prediction-identification landscape revealed a dichotomy between phenotypes suited to identifying individuals and phenotypes that could explain individual variation in behavior (Figure 5). High-resolution structural connectomes performed well at both tasks. When comparing different resolutions, we found that vertex-based phenotypes, in general, improve identification and prediction performance over their atlas-based counterparts for nearly all behavioral domains and phenotypes (refer to Figure 3). This suggests that a higher resolution captures additional detail to enable greater task accuracy (Figure 4).

## Acknowledgements

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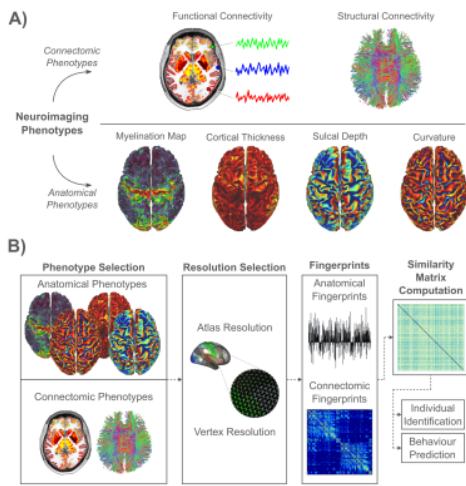
doi: 10.4225/49/58ead90dceaaa.

## Figures

Figure 1: Study overview. A) Neuroimaging-derived phenotypes arranged according to cortical structure (bottom) and connectivity (top). B) Schematic of methodology. First, a neuroimaging-derived phenotype is selected. Second, the selected phenotype is either mapped at the resolution of voxels/vertices, or a regional atlas. Third, the selected phenotype is represented as a fingerprint for each individual. Finally, the similarity in fingerprints is computed between pairs of individuals. The similarity matrix is used for individual identification and behavior prediction.
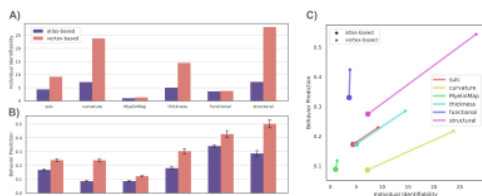


Figure 2: Performance of neuroimaging-derived phenotypes in individual identification and prediction of individual variation in behavior. A) Individual identification is the effect size (Cohen's d) difference of the phenotypic similarity of the true pairs compared to the false pairs. B) Average variance explained by VCM for components of cognition and behavior. C) A and B combined to yield a two-dimensional prediction-identification landscape. Phenotypes measured at the resolution of vertices (stars) and atlas-based regions (circles) are shown.
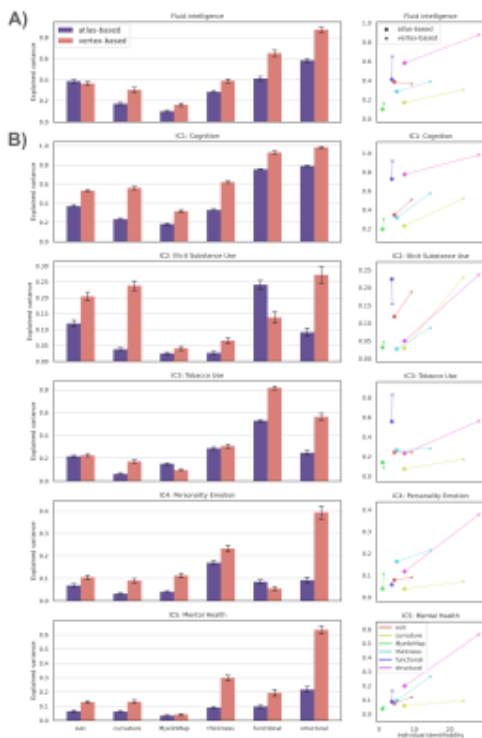


Figure 3: Behavior interpretation. A) Variance explained by VCM for the fluid intelligence measure from HCP dataset which was used in previous functional fingerprinting studies. B) Detail of VCM results for all components of cognition and behavior (cognition, illicit substance use, tobacco use, personality-emotion, and mental health). The line plots present the prediction-identification landscape for each phenotype. Note that the horizontal and vertical axes are shared in all plots.
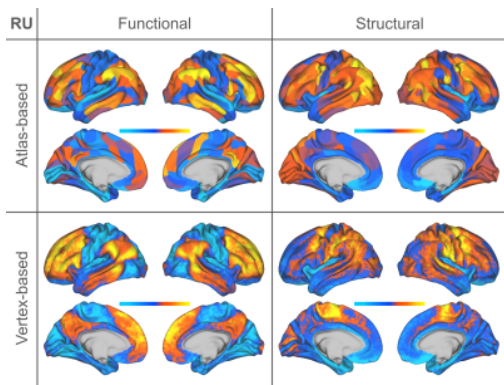
Figure 4: Measures of regressed uniqueness (RU). These measures are derived by regressing out false pair similarities from the true pair similarities in functional and structural connectomes. The spatial overlap between SC and FC results present how highly unique FC patterns arise from the underlying unique SC patterns. The intricate detail provided in the higher resolution contains information such as intensity and gradual change which is lost in the pixelated atlas-level presentation.
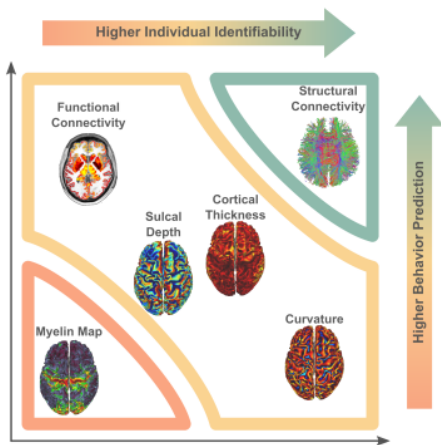


Figure 5: Neuroimaging-derived phenotypes arranged in a two-dimensional space, where the horizontal and vertical axes, quantify performance in behavior prediction (variance explained) and individual identification (Cohen's d), respectively. Structural connectivity performs well for both tasks, whereas a dichotomy is evident for the other measures. This shows a trade-off where high performance in one dimension results in low performance in the complementing dimension.