A Novel Bayesian Semi-parametric Model for Learning Heritable Imaging Traits

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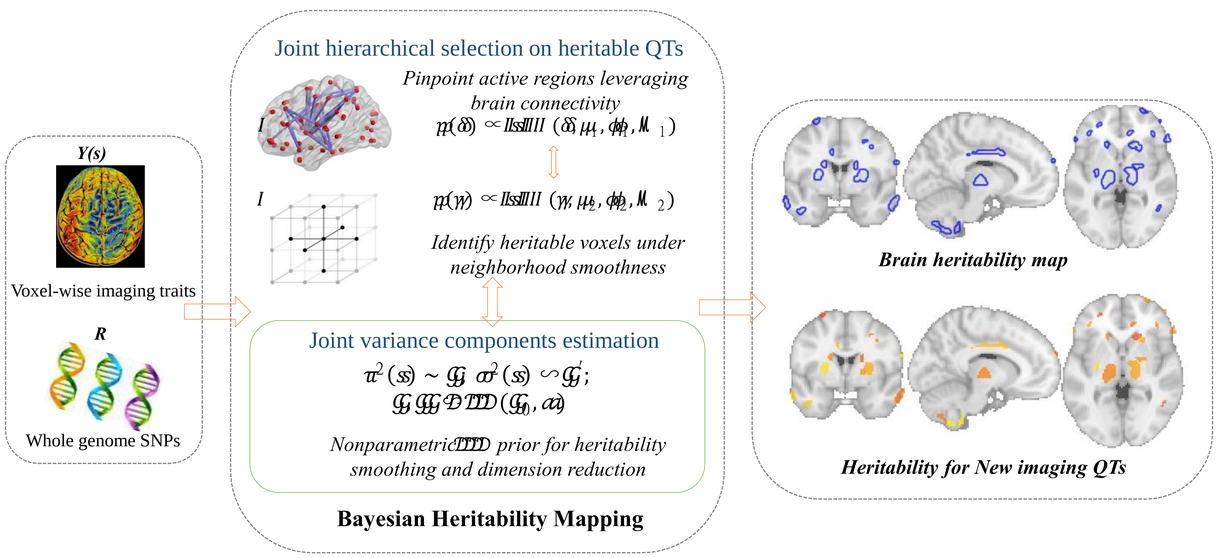
1. Introduction

Heritability analysis is an important research topic in brain imaging genetics. Its primary motivation is to identify highly heritable imaging quantitative traits (QTs) for subsequent in-depth imaging genetic analyses. Most existing studies perform heritability analyses on regional imaging QTs using predefined brain parcellation schemes such as the AAL atlas. However, the power to dissect genetic underpinnings under QTs defined in such an unsupervised fashion is largely deteriorate with inner partition noise and signal dilution. To bridge the gap, we propose a new semi-parametric Bayesian heritability estimation model to construct highly heritable imaging QTs. Our method leverages the aggregate of genetic signals to imaging QT construction by developing a new brain parcellation driven by voxel-level heritability. To ensure biological plausibility and clinical interpretability of the resulting brain heritability parcellations, hierarchical sparsity and smoothness, coupled with structural connectivity of the brain, are properly imposed on genetic effects to induce spatial contiguity of heritable imaging QTs.

2. Methods



Our overarching goal is to construct more powerful neuroimaging endophenotypes with strong genetic dissection power based on an innovative ``brain heritability map''. We propose a Bayesian semi-parametric model to jointly estimate voxel-specific heritability over whole brain imaging traits. Within the Bayesian paradigm, a hierarchical Ising-Spike-and-Slab prior is used to simultaneously impose sparsity on heritabilities at 1) brain regions while accounting for correlations induced by brain structural connectivity; 2) voxels while considering the dependency among adjacent voxels. To enhance biological insight and reduce parameter space, we further assign a Dirichlet process prior on the genetic and environmental variance components, so that each of them are identical within a contiguous brain area. Based on the result, a brain heritability map can be constructed directly with the new imaging phenotype defined under the ``active'' subregions; and the heritability for each of them is also estimated.

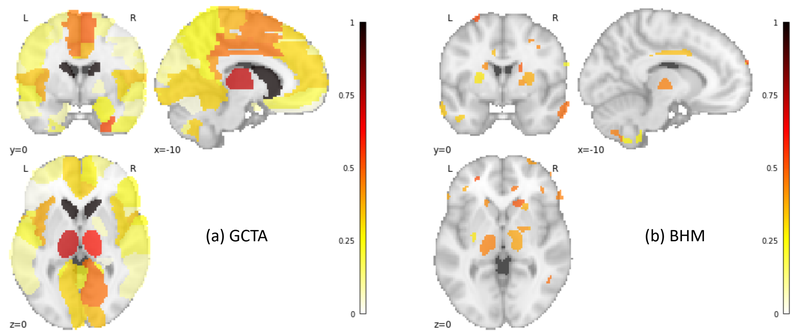
3. Results

The neuroimaging and genotypinig data used in this work were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database.

Table 1 shows the heritability estimation results of comparing the proposed BHM model and the traditional GCTA model, including 47 BHM-identified ROIs. For most of these ROIs, BHM was able to identify new imaging QTs with higher heritability than the GCTA-estimated heritability for the entire ROI based average measure.

Region	Left Hemisphere			Right Hemisphere		
	GCTA	BHM	N_{Voxels}	GCTA	BHM	N_{Voxels}
Precentral				0.063	0.443	281
Frontal_Sup	0.124	0.532	352	0.119	0.409	429
Frontal_Sup_Orb	0.031	0.533	82	0.000	0.507	42
Frontal_Mid	0.109	0.321	331	0.003	0.446	259
Frontal_Inf_Oper	0.210	0.403	148	0.098	0.539	174
Frontal_Inf_Tri	0.014	0.390	194	0.223	0.452	564
Frontal_Inf_Orb				0.261	0.613	118
Rolandic_Oper				0.333	0.442	75
Frontal_Sup_Medial	0.311	0.323	264	0.265	0.421	227
Rectus	0.184	0.400	32	0.154	0.321	55
Cingulum_Ant				0.328	0.473	113
Cingulum_Mid	0.470	0.353	108			
Cingulum_Post				0.398	0.678	55
ParaHippocampal				0.240	0.487	41
Occipital_Inf				0.244	0.343	35
Postcentral	0.090	0.485	289	0.123	0.226	235
Parietal_Inf				0.336	0.554	66
SupraMarginal				0.172	0.428	62
Angular				0.028	0.391	56
Caudate	1.000	0.433	117	1.000	0.509	273
Putamen	0.000	0.288	312	0.000	0.377	356
Pallidum				0.068	0.419	75
Thalamus	0.720	0.445	446	0.613	0.391	324
Temporal_Pole_Sup	0.196	0.324	80	0.257	0.424	330
Temporal_Mid	0.091	0.340	123	0.085	0.478	298
Temporal_Pole_Mid	0.052	0.288	203	0.026	0.482	228
Temporal_Inf	0.000	0.323	101			
Cerebelum_8	0.322	0.450	409	0.456	0.369	150
Cerebelum_9	0.000	0.265	283	0.111	0.382	121
Cerebelum_10	0.285	0.132	58			

Figure 2 shows the heritability maps estimated by (a) the conventional GCTA method and (b) the proposed BHM method.



4. Conclusions

We have proposed a new semi-parametric Bayesian heritability estimation model to construct highly heritable and biologically meaningful imaging quantitative traits (QTs).

Our method leverages the aggregate of genetic signals to imaging QT construction by developing a new brain parcellation driven by voxel-level heritability. To ensure biological plausibility and clinical interpretability of the resulting brain heritability parcellations, hierarchical sparsity and smoothness, coupled with structural connectivity of the brain, have been properly imposed on genetic effects to induce spatial contiguity of heritable imaging QTs.

Using the ADNI imaging genetic data, we have demonstrated the strength of our proposed method, in comparison with the standard GCTA method, in identifying highly heritable and biologically meaningful new imaging QTs.

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