GAMing THE BRAIN: INVESTIGATING THE CROSS-MODAL RELATIONSHIPS BETWEEN FUNCTIONAL CONNECTIVITY AND STRUCTURAL FEATURES USING GENERALIZED ADDITIVE MODELS

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ABSTRACT

- Proposed a novel and easily implemented analysis approach aimed at explaining the variation in functional connectivity of the brain by integrating local structural factors such as anatomical morphology summaries, voxel intensity, diffusion-weighted information, and geographic distance in a generalized additive model (GAM) framework.
- Our approach can be performed in template space, as well as subject (vertex) space, thereby accounting for inter-subject differences.

METHODS

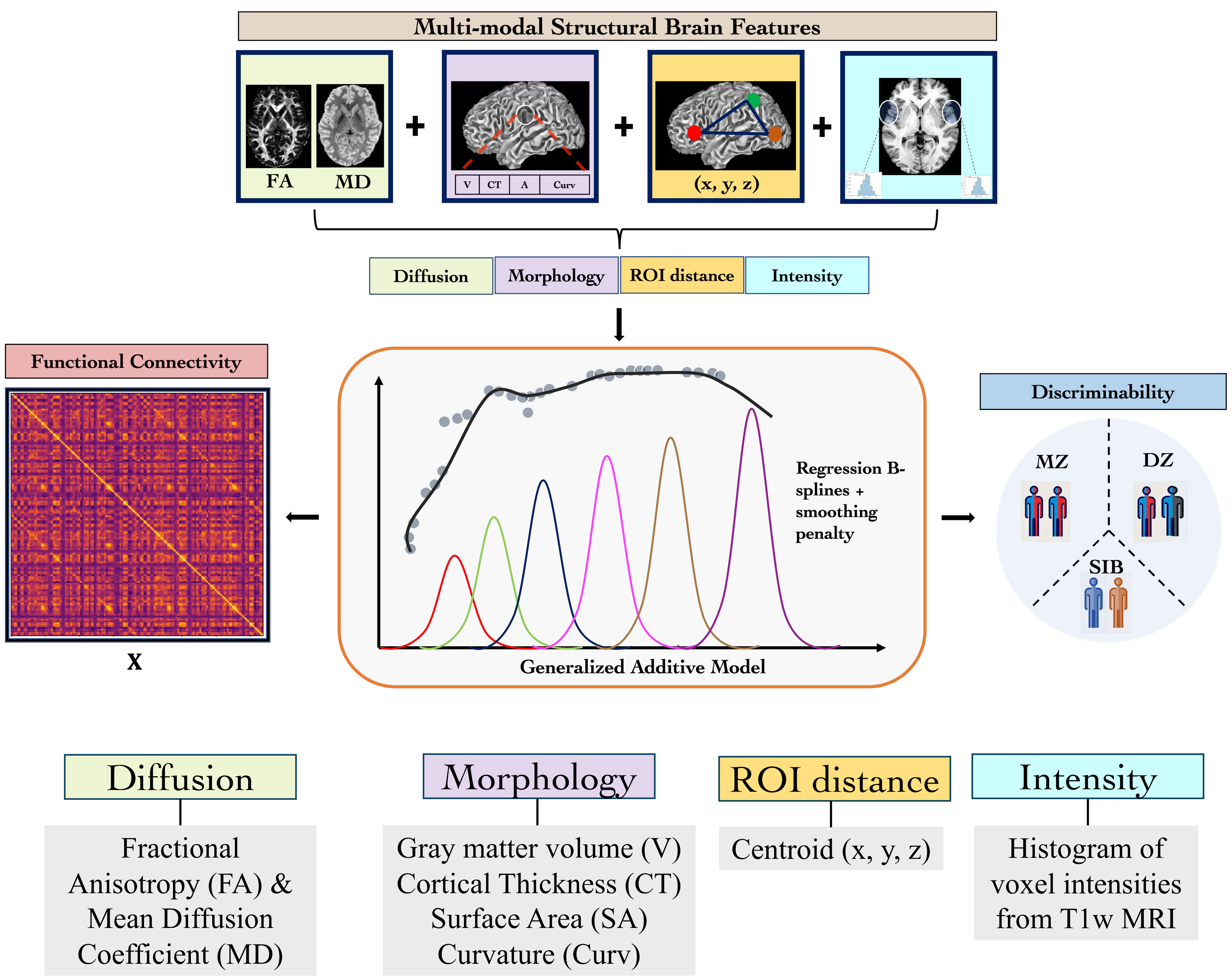

Fig 1. Integration of multi-modal structural brain features with functional connectivity data for discriminability analysis.

$$\mathbf{X}_s(i,j) = \alpha + f_1(\text{Diffusion}(i,j)) + f_2(\text{Morphology}(i,j)) + f_3(\text{Distance}(i,j)) + f_4(\text{Intensity}(i,j)) + \epsilon_s(i,j).$$

- α – intercept term
- $f_n(\cdot)$ – penalized regression B spline functions on the structural covariates
- ϵ_s – error term

$$\delta_{\text{group}} = \underbrace{\frac{1}{P(P-1)T^2(T-1)}}\sum_{p=1}^{P}\sum_{\substack{q=1\\ q\neq p}}^{P}\sum_{i=1}^{T}\sum_{j=1}^{T}\underbrace{\mathbb{I}\{d(Z_{p,i}, Z_{p,j}) < d(Z_{p,i}, Z_{q,j})\}}$$

P – sample size
T – number of repeated measurements

$Z_{\cdot,\cdot}$ – vector of measurement values
$d(\cdot)$ – distance metric

DATA

- Human Connectome Project (HCP) – 900 subject release
- Data preprocessed through HCP preprocessing pipeline
- Atlas space: Destrieux atlas with 148 brain ROIs
- Vertex space: vertices sampled through spatial stratified sampling defined by the atlas in subject space

RESULTS

Partial Dependence (PD) Analysis:

Visualize the effect of a single structural covariate on the predicted outcome of functional connectivity:

$$PD(X_k) = E_{X_{\sim k}}[f(X_k, X_{\sim k})]$$

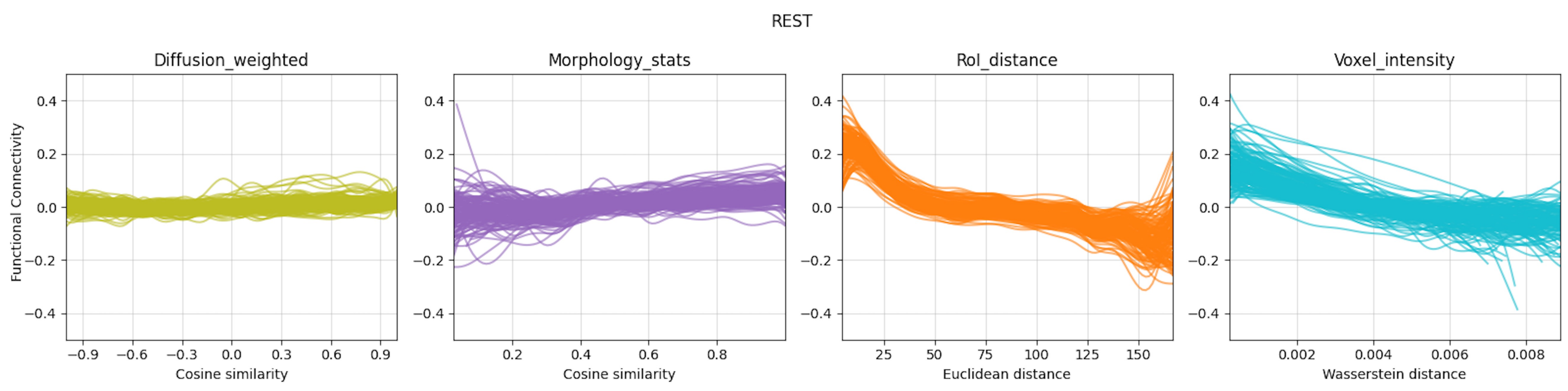

Fig 2. Partial dependence plots of structural features against functional connectivity values for resting state in template space.

Discriminability Analysis:

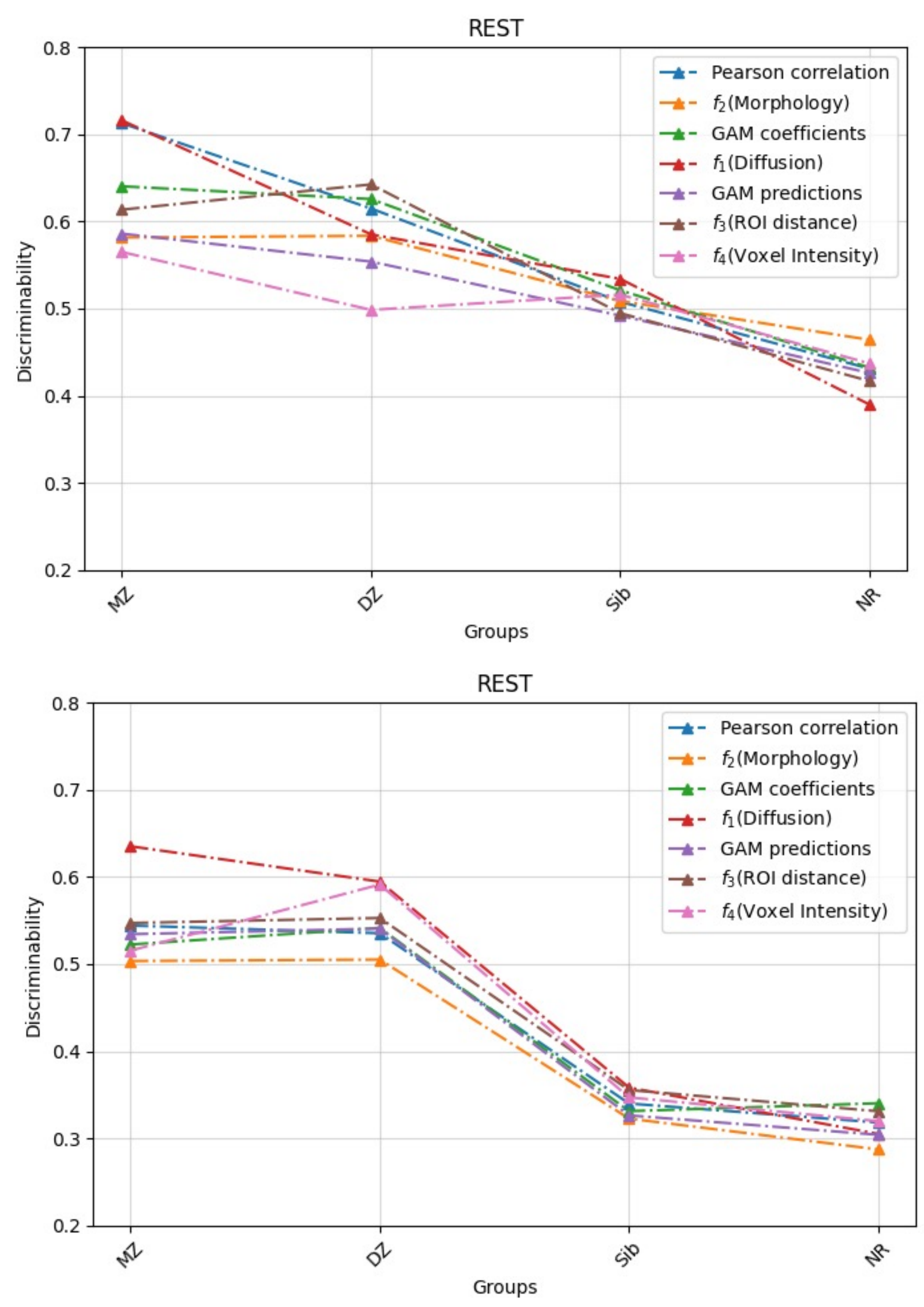

Fig 3. Discriminability analysis comparing MZ, DZ, SIB, and NR individuals for resting state in **Top**: template and **Bottom**: vertex (subject) spaces.

- Utilized the spline coefficients of structural covariate from partial dependence analysis (f_n), model summary statistics, GAM predictions and Pearson correlations to compute the distance $d(\cdot)$ in discriminability analysis, thereby combining PD analysis to derive the δ_{group} scores shown in Fig 3.
- Higher values of δ indicate greater repeatability of measurements.

CONCLUSION

- Introduced a unique way for accommodating inter-individual variability—a crucial aspect frequently neglected in traditional analyses.
- Downstream task highlights our framework's efficacy in discriminating variances within brain connectivity configurations.

Acknowledgements: This work was supported by National Institutes of Health R01 EB029977 (PI Caffo) and R01 HD108790 (PI Venkataraman)