Brain Mapping of Behavioral Domains Using Multi-Scale Networks and Canonical Correlation Analysis

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Simultaneous mapping of multiple behavioral domains into brain networks remains a major challenge. Here, we shed some light on this problem by employing a combination of machine learning, structural and functional brain networks at different spatial resolutions (also known as scales), together with performance scores across multiple neurobehavioral domains, including sensation, motor skills, and cognition. Provided by the Human Connectome Project, we make use of three cohorts: 640 participants for model training, 160 subjects for validation, and 200 subjects for model performance testing thus enhancing prediction generalization. Our modeling consists of two main stages, namely dimensionality reduction in brain network features at multiple scales, followed by canonical correlation analysis, which determines an optimal linear combination of connectivity features to predict multiple behavioral performance scores. To assess the differences in the predictive power of each modality, we separately applied three different strategies: structural unimodal, functional unimodal, and multimodal, that is, structural in combination with functional features of the brain network. Our results show that the multimodal association outperforms any of the unimodal analyses. Then, to answer which human brain structures were most involved in predicting multiple behavioral scores, we simulated different synthetic scenarios in which in each case we completely deleted a brain structure or a complete resting state network, and recalculated performance in its absence. In deletions, we found critical structures to affect performance when predicting single behavioral domains, but this occurred in a lesser manner for prediction of multi-domain behavior. Overall, our results confirm that although there are synergistic contributions between brain structure and function that enhance behavioral prediction, brain networks may also be mutually redundant in predicting multidomain behavior, such that even after deletion of a structure, the connectivity of the others can compensate for its lack in predicting behavior.

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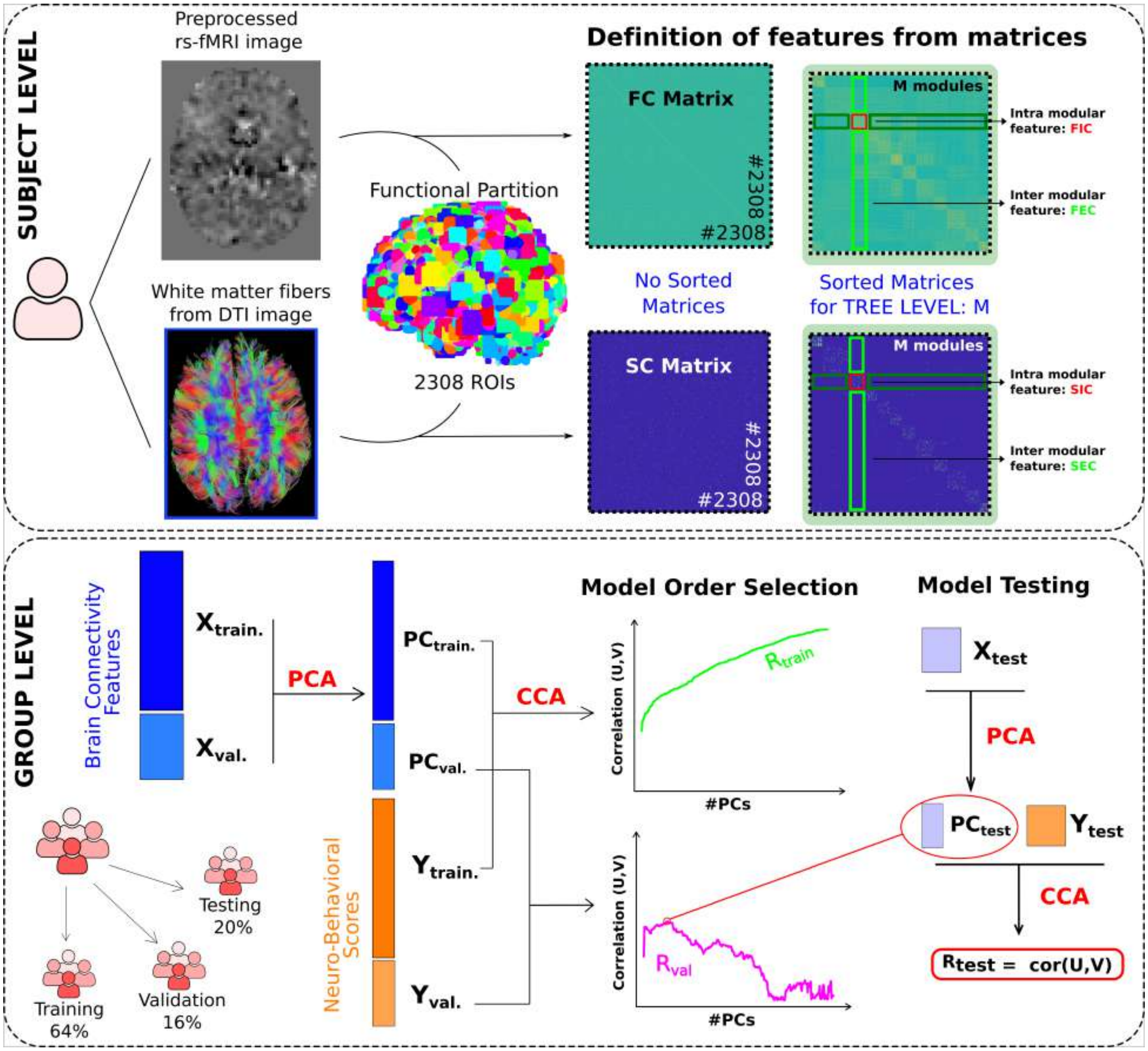

FIG. 1: **Brain mapping of neuro-behavioural scores using multimodal and multiscale networks through canonical correlation analysis.** Subject level: FC and SC brain networks were built respectively from two data modalities: resting functional imaging (rs-fMRI) and diffusion tensor imaging (DTI). An initial functional brain partition of 2,308 microregions (ROIs) was built, which represents the lowest level (the one with highest spatial resolution) of our hierarchical partitioning. For the different M levels in the hierarchical tree (here, we varied M from 20 to 1,000), we built for each module in the M level four classes of connectivity features: FIC, FEC, SIC and SEC. This procedure provided a total number of 5,208 multi-scale connectivity features for each subject, 2,587 structural and 2,621 functional, which were used for the following analyses. Group level: Three different cohorts

have been used, Training, Validation and Testing. The training and validation datasets were used for selecting the number of principal components (PCs) to reduce the original X dimensionality, containing all connectivity-features. Such a number, considered here as the model order, will be finally used to predict the neuro-behevioural scores (Y) by means of CCA in the test dataset, which provides the final performance (measured by R) in the association between connectivity and behaviour.

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