Structure-function dependencies as informative features for brain decoding and fingerprinting

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***Abstract*— Functional magnetic resonance imaging has proven useful to decode task-specific brain activity and act as brain fingerprints, that is, allowing accurate identification of individuals within a large group. In this context, the relationship between functional activity and the underlying structural wiring, extracted from diffusion-weighted magnetic resonance imaging, can be a new imaging-based biomarker characterizing tasks and individuals. To investigate this, we used a recent graph signal processing framework to quantify the regional function-structure dependencies through the structural decoupling index (SDI), in 100 unrelated healthy volunteers from the Human Connectome Project, scanned both during resting-state and seven different tasks. SDI values of different tasks and subjects could be leveraged for accurate classification using linear discriminant analysis. The accuracies were very high and better than the ones obtained with functional connectivity alone. Further, we could identify two distinct brain networks, including most discriminative regions for task decoding and fingerprinting, respectively. These results show that rich information is contained in brain function-structure relationships, and that these provide new promising signatures of tasks and subjects.**

Keywords — decoding, fingerprinting, fMRI, structural decoupling index, graph signal processing

I. Introduction

The relation between brain functional activity and structural architecture remains to date an open question in neuroscience. In our previous study, we introduced the structural decoupling index (SDI); i.e., a regional measure defined within a graph signal processing (GSP) framework [1] and quantifying the degree of structure-function coupling for each brain region [2]. In this context, the structural connectome obtained from diffusion-weighted magnetic resonance imaging (MRI) serves as graph, and the functional MRI activity defined at the same nodes (brain regions) as graph signal. During resting-state, the SDI showed a very specific spatial distribution, spanning from lower-level sensory and somatomotor functional areas, with function highly aligned to the structure underneath, to higher-level fronto-parietal ones, more independent from the structure [2]. Here, we investigate for the first time how these structure-function dependency profiles change across tasks and individuals. To this aim, we assess the classification performance of SDI values in task and subject identification, evaluating therefore the decoding and fingerprinting value of such measure. In fact, functional brain activity is known already for the ability to well distinguish between both tasks [3] and individuals [4], offering a brain signature able to recognize whether a subject is at rest or performing a given task (decoding), as well as to identify an individual within a large group (fingerprinting). In a seminal paper from Finn and colleagues [5], functional connectivity profiles were used to successfully classify subjects across resting-state test-retest sessions, and even between task and rest conditions. The fronto-parietal network emerged as the main contributor to subject discrimination and was shown to predict individual cognitive behavior (level of fluid intelligence). In parallel, brain structural features were also used in the past for brain fingerprinting [6].

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However, these features analyze either structure or function alone, and the characterization of the structure-function dependency profiles has remained so far unexplored.

II. Methods

A. Image Preprocessing

100 unrelated healthy subjects from the Human Connectome Project (HCP) were included in the study (ethical approval was obtained within the HCP). Functional MRI with resting-state (RS) and 7 tasks (Emotion, Gambling, Language, Motor, Relation, Social, Working Memory), as well as diffusion-weighted MRI sequences, were pre-processed with state-of-the-art pipelines, in order to obtain regional functional timecourses and their structural connections, based on a parcellation with 360 cortical [7] and 19 subcortical [8] areas ($N_{ROI} = 179$). Structural connectomes were obtained as the number of reconstructed fibers between two regions normalized by the sum of the region volumes. RS data were filtered in the range [0.01-0.15] Hz. To remove the effect of the paradigm on task data, paradigms were regressed out trial by trial. Functional connectivity (FC) between region pairs was obtained as the Pearson's correlation between nodal timecourses. The nodal FC strength was defined as the sum of the functional connectivity values of one region with all the other brain regions.

B. GSP framework for SDI computation

The GSP framework detailed in [2] was used to obtain the SDI, for each subject and acquisition. In particular, the average structural connectome across the population is considered as adjacency matrix A and symmetrically normalized with respect to the degree matrix to obtain A_{symm}.

Structural harmonics u_k are then obtained by eigendecomposition of the structural Laplacian $L = I - A_{symm}$:

$$LU = U\Lambda, \tag{1}$$

where each eigenvalue $[\Lambda]_{k,k} = \lambda_k$ can be interpreted as spatial frequency of the corresponding structural harmonic (eigenvector) u_k. Functional data s_t at each timepoint t is then projected onto the structural harmonics by assessing the spectral coefficients

$$\widehat{s_t} = U^T s_t, \tag{2}$$

and filtered into two components with ideal low- and high-pass filters; i.e., a coupled one obtained as $s_t^C = U^{(low)}\widehat{s_t}$ and a decoupled one as $s_t^D = U^{(high)}\widehat{s_t}$, respectively ($U^{(low)}$ being a matrix with the c first eigenvectors complemented by zeros, and $U^{(high)}$ being a matrix with c first columns of zeros followed by the remaining last eigenvectors). To avoid task-bias, the cut-off to filter functional activity based on structural harmonics was set to $c=50$ spectral components for all acquisitions. Finally, coupling and decoupling were quantified for each brain region as the $l2$-norm across time of the coupled and decoupled signal portions s_t^C and s_t^D, and the SDI was computed as their ratio.

C. Brain patterns of task decoding and fingerprinting

A two-factor (subject and task) ANOVA on regional SDI values was performed to identify brain patterns of task and subject main effects (decoding and fingerprinting patterns, respectively; significant F-values with $p < .05$, accounting for Bonferroni correction across regions).

D. Brain decoding: task classification

A linear discriminant analysis (LDA) with $N_{BS} = 8$ classes was performed to classify a brain state bs ($bs = 1, \dots, N_{BS}$, i.e. resting-state or one of the 7 tasks) based on the feature matrix X of SDI patterns for all subjects and acquisitions. LDA identifies $N_{BS} - 1$ meaningful discriminative directions, each associated to a N_{ROI}-dimensional vector of weights which identifies brain regions mostly contributing to the classification in that LDA direction. The projection of original data X onto the $N_{ROI} \times N_{BS} - 1$ matrix W of weights leads to the LDA scores LD:

$$LD = X \cdot W, \tag{3}$$

which maximize the inter-class variability while minimizing the intra-class one, and are used for the classification. A *leave-one-subject-out* (100-fold) cross-validation was implemented, where the acquisitions from one subject were excluded for each fold. For comparison, the same classification was performed on a nodal measure of FC, namely FC node strength.

E. Fingerprinting: subject classification

A second LDA with $N_S = 100$ classes was performed to classify individuals, based on SDI values of all acquisitions. Different classification settings were explored: (1) classification of a subject s doing a specific task bs, based on all other tasks/individuals. This was implemented with a *leave-one-subject's-task-out* (800-fold) cross-validation, where the N_E entries (two different encoding directions) of subject s doing task bs were excluded for each fold; (2) classification

of a subject s doing a specific task bs, based on the entries related to all subjects during the remaining $N_{BS} - 1$ tasks; i.e., a *leave-one-task-out* (8-fold) cross-validation where all entries from task bs are excluded at every fold. For comparison with purely functional data, the same classifications were performed on FC node strength.

III. Results

A. Brain decoding and fingerprinting networks

The two-factor ANOVA yielded two very distinct and spatially specific brain patterns (Fig. 1), characterized by a significant effect for either decoding (task-effect) or fingerprinting (subject-effect), respectively (F-test, only nodes with significant F-values are visualized as non-zeros in Fig. 1, with p<.05, Bonferroni-corrected for the number of brain regions). The brain decoding pattern (Fig. 1a) clearly involves more prominently regions of task-related networks, in particular visual and somatomotor networks. On the contrary, the brain fingerprinting pattern (Fig. 1b) was spatially more spread, but concerned mainly the posterior parietal cortex, including fronto-parietal regions, consistently with what was found previously [8], but also visual, somatomotor and dorsal attention networks.

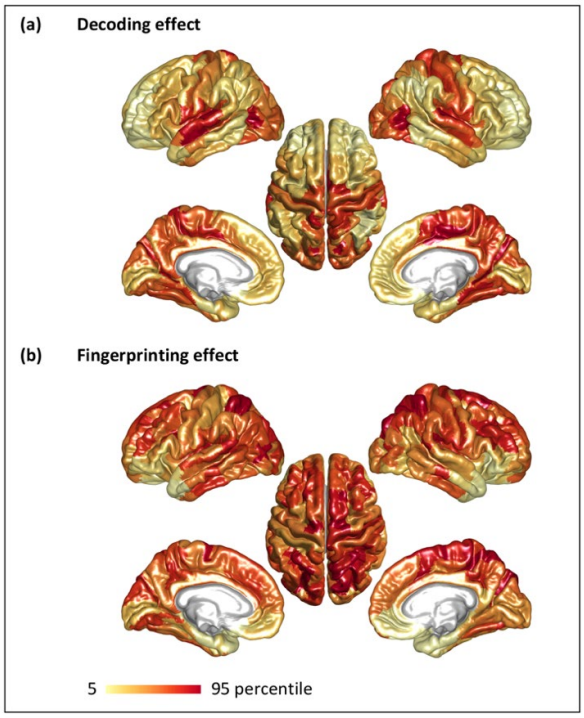

Fig. 1. **Brain networks of task (*brain decoding*) and subject (*brain fingerprinting*) main effects on structure-function dependency.** Two-Factors ANOVA, significant F-values, p<.05 Bonferroni corrected.

B. Brain decoding

An accuracy of 0.75 (against a chance-level accuracy of 0.125) was obtained with a *leave-one-subject-out* cross-validation setting. The same classification performed on FC nodal strength values led to a lower accuracy of 0.52, showing that structure-function dependencies alone are able to well characterize both resting-state and the different task conditions and outperform a nodal measure based on functional data only.

The LDA outputs seven meaningful discriminant directions, ordered by their discriminative power, and Fig. 2a shows the projection of the data onto the first four (i.e., the LDA scores). Notably, SDI values allow to separate very well not only resting-state from task, but also among different tasks, while this separation is less obvious when LDA is performed on FC nodal strength values (Fig. 2b).

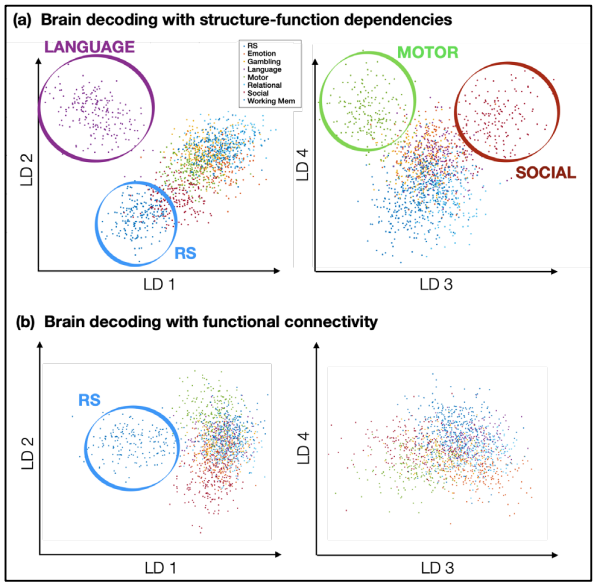

Fig. 2. **Brain decoding.** Projection of the data onto the first 4 LDA discriminant directions, for (a) Structural-Decoupling Index and (b) functional connectivity node strength values. The higher performance of brain decoding based on structure-function interplay (accuracy=0.75) vs. functional connectivity (accuracy=0.52) is visually remarkable by the data projection in the LDA reduced space: different tasks are much better separated in (a) with respect to (b), which discriminates more successfully only resting-state from all other tasks. RS=resting-state; Working Mem=Working Memory.

C. Individual fingerprinting

In addition to characterizing different task-related states, structure-function dependencies revealed to be highly specific to different individuals, allowing for the identification of subjects with a perfect accuracy of 1 (both in a *leave-one-subject's-task-out* and in an 8-fold cross-validation setting), slightly higher than the performance of FC nodal strength values for the same classifications (0.98, for both settings).

IV. Discussion

Brain structure-function dependencies showed to be specific both to the functional state (decoding) and to the individual (fingerprinting). Concerning decoding, SDI proved the capability of discriminating very well not only rest from task, but also among different functional tasks, outperforming a purely functional nodal measure (FC node strength). In fact, even if we can assume brain structure will not change across different task-related states in the same individual, the way brain function couples to the underlying structure is likely to adapt to the demands of the task. Further, having regressed out task paradigms, we can remark that the classification captures differences in functional states driven by the specific cognitive task, but not "artificially" induced by the paradigm.

Further, the structural decoupling index revealed also able to identify individual subjects in a group with near-perfect accuracy, indicating that, despite it changes depending on the task demands, the pattern of structure-function coupling remains an intrinsic feature (or *fingerprint*) of an individual's brain organization, similarly as it happens for brain function [4, 5, 9].

Contributions of brain regions to subject and task identification were found not uniformly distributed across the cortex: two clearly distinct networks were highlighted, one for brain fingerprinting and one for task decoding (see Fig. 1). The decoding pattern mainly involved lower-level primary sensory regions, such as somatomotor and visual networks, where structure-function coupling appears stronger both in rest and task. The fingerprinting pattern, instead, shows that individual uniqueness of structure-function dependencies is mainly expressed in parietal, dorsolateral prefrontal and association cortices including the visual association and supplementary motor areas. This involves transmodal association cortices including the fronto-parietal network, which have been reported to contribute to subject identification from functional connectivity [5]. However, this pattern is broader and includes both regions that are coupled and regions that are decoupled with structure.

Future research addressing the correlation of structure-function dependencies with cognitive measures will help elucidating the behavioral relevance of these findings.

V. Conclusion

We expanded here previous research by identifying the fingerprinting and decoding potential of structure-function dependencies. Specifically, we showed that the structural decoupling index characterizes both different tasks and individuals, ameliorating the performance of a purely functional measure ignoring the underlying brain architecture.

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