Introduction (1228)

Mapping the behavioral impact of brain lesions is of crucial importance for clinical practice. Regardless of the cause of the lesion, its size or the precise location, accumulated evidence in recent years has pushed forward the connectome hypothesis to show that the belonging of a lesion to a specific network can predict a multitude of responses in the patient across behavioral, cognitive, or sensory-motor domains. Lesion network mapping (LNM) is a successful technique for mapping symptoms to neural networks after acquired brain injury. Beyond lesion characteristics such as its etiology, size or location, LNM has shown that when a subgroup of patients has common symptoms after an injury this is because their lesions are part of the same network, thus linking symptoms to specific networks. Here, we extend LNM according to two strategic avenues. Firstly, by proposing a multimodal approach in which we introduce a combination of both structural and functional networks to predict behavior. Secondly, by assessing behavioral performance using a combination of several multi-domain scores. For this purpose, we employed a canonical correlation analysis to link multi-domain behavior to different lesion connectivity maps.

Methods (1154)

We analyzed N=54 first-stroke patients (25 males) with a mean age of 68.78 ($\sigma = 13.98$; range 28 – 92 years). Every patient was assessed with the same four tests: Action Research Arm Test (ARAT) and Fugl-Meyer assessment - upper extremity (FMA-UE) as motor variables; and Erasmus-modified Nottingham Sensory Assessment (Em-NSA) and perceptual threshold of touch (PTT) as somatosensory variables.

We build structural connectivity (SC) and functional connectivity (FC) maps of each patient-lesion mask using data of the Human Connectome Project with 1000 healthy participants. We reduced the dimension of the lesion connectivity maps using Principal Component Analysis (PCA) and associated the multimodal imaging components to the sensory-motor scores applying a Canonical Correlation Analysis (CCA). In order to overcome the overfitting, we performed leave-one-out cross-validation. The methodology was performed for SC and FC separately (unimodal analyses) and combined by spatial concatenation of the SC and FC matrices (multimodal analysis), followed by PCA and using the obtained mixed components to apply CCA similarly as we did for the unimodal cases.

Results (901)

Our results are three-fold. Firstly, the multimodal analysis reveals that functional connectivity maps contributed more than structural connectivity maps in the optimal prediction of sensorimotor behavior. Secondly, the maximal association solution between behavioral outcome and multimodal lesion connectivity maps provided equally contribution of sensory and motor coefficients, in contrast to the unimodal analyses where the sensory contribution dominated in both structural and functional maps. Finally, when looking at each modality individually, the performance of the structural connectivity maps strongly depended on whether sensorimotor performance was corrected for lesion size (thus eliminating the effect that larger lesions produce higher sensorimotor dysfunction). In contrast, the maps of functional connectivity provided similar performance with and without correcting for lesion size.

Conclusions (518)

The application of our multimodal LNM approach to predict multidomain sensorimotor behavior, supports the synergistic and additive features that different types of brain networks have on patient's outcome after brain injury, thereby making the whole more than the sum of its parts. Moreover, when the patient's behavior is assessed across multiple domains of cognitive, sensory and motor function, our methodology combining structural and functional maps appears most suitable when assessing such multidomain outcomes.

TOTAL: 3801/4000

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Figure

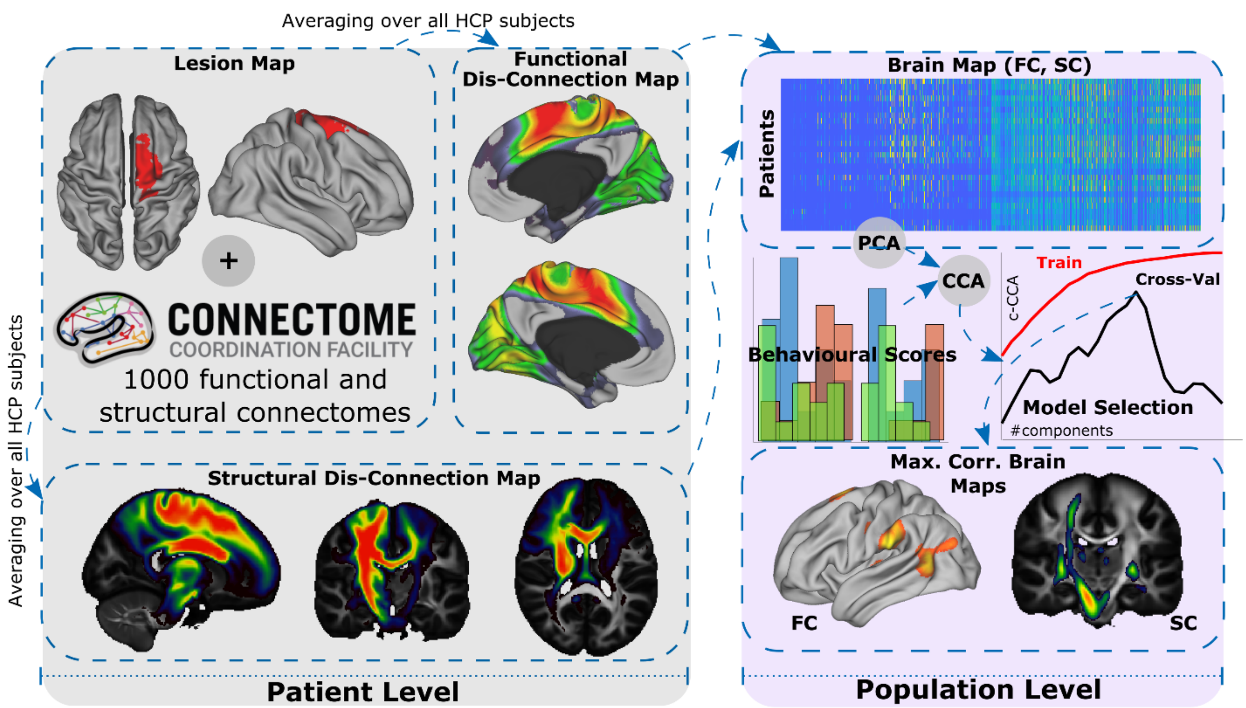

Figure 1. Pipeline for multimodal lesion network mapping, and its association to behavioral outcome after stroke through Canonical Correlation Analysis (CCA). At the patient level (gray shadow), brain lesion masks are used as seed regions for calculating the functional correlation maps (applying seed-based correlation analysis using the segmented lesion as the seed for each subject of the HCP) and structural correlation maps (applying tractography from the segmented lesion to the rest of the brain in each subject of the HCP) from a group of N=1000 healthy control participants from HCP. After averaging over all participants in the HCP dataset (see Methods for details), we obtained for each patient the functional disconnection maps, accounting for the FC impact of the lesion disconnection, and

similarly for SC, the structural disconnection maps. At the population level (purple shadow), a matrix with dimensions (# of stroke patients) x (# of voxels) per modality map (FC or SC) is built and reduced using PCA, which returns a new matrix with dimensions (# of patients) x (# of principal components), the PCA components considered here as the brain map features. The association between SC and FC features and behavioral scores is obtained applying CCA. As the number of features increases, the correlation between features and behavior, represented here as c-CCA increases up to values near to 1 (red curve, Train), dealing to overfitting. Cross-validation techniques can overcome this problem (for details see Methods). For the maximum CCA correlation value in the cross-val curve (black), we built brain maps of those components producing maximum performance. The maps can be obtained in a single modality, here shown FC or SC, or in a combination of them (not shown here but implemented in this study). Abbreviations: FC: functional connectivity; SC: structural connectivity; PCA: principal component analysis; CCA: canonical correlation analysis.