Functional Connectivity Changes in the Presence of Brain Tumors

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PURPOSE

As part of the Software for the Use of Multi-Modality images in External Radiotherapy (SUMMER) project, one of the specific aims is to investigate brain tumor patients with resting state fMRI (rs-fMRI). This is done to study changes occurring in rs-networks and their functional connectivity due to tumor burden and chosen treatment method. In this work, connectivity changes between different networks in ten post-surgical patients were studied and compared to healthy subjects based on study specific node selection. We hypothesized for a decreased connectivity between network nodes in the patients compared to healthy subjects.

METHODS

To assess functional networks, 3 five minute rs-sequences (EPI, TR/TE=2.00s/30ms) were acquired with 3T Philips Achieva from 10 glioblastoma multiforme patients (4 female/6 male, age=54.4) and 5 healthy subjects (5 male, age=32.2). The data were processed using FSL[1] and MATLAB. Preprocessing included motion correction (MCFLIRT), brain extraction, smoothing (5mm) and intensity normalization before running MELODIC ICA to identify rs-networks. Registrations between functional networks and anatomical images (T1/MNI) were conducted using FSL's FLIRT tool (6/12 DOF).

RESULTS

Dorsal attention (DAN), sensorimotor (SMN), visual and default-mode (DMN) networks were identified from ICs for all the patients. Voxel consistency maps for each network were obtained by summing up thresholded and binarized individual IC's from which percentage consistencies were calculated. Based on these maps (Fig.1) clusters representing separate nodes were identified and thus 15 reproducible nodes were selected and compared to previous studies[2]. A measure of functional connectivity based on the Pearson correlation coefficient was computed between BOLD time series on each node and a cross-correlation matrix was obtained for each patient and control. Across patients and controls, Z-scored connectivity matrices were computed by contrasting the correlation value of each voxel with the average correlation in each node (Fig.2).

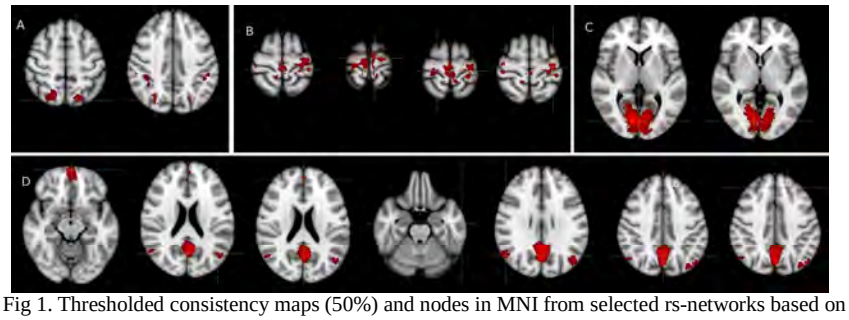

Fig 1. Thresholded consistency maps (50%) and nodes in MNI from selected rs-networks based on ICA. A) DAN: Left Posterior Intra Parietal Sulcus (-15, -73, 53), Right Posterior Intra Parietal Sulcus (26, -71, 39), B) SMN: Right Supplementary Motor Area (6, -31, 66), Left Supplementary Motor Area (-8, -15, 73), Right Central Sulcus (19, -25, 69), Left Central Sulcus (-34, -20, 64), C) VISUAL: V1 left (1, -81, 4), V1 right (10, -80, 1), D) DMN: Ventral Medial PreFrontal Cortex (0, 64, -13), Left Angular Gyrus (-43, -67, 21), Right Medial Prefrontal Cortex (-1, 51, 21), Left Inferior Temporal Gyrus (-60, -13, -23), Right Angular Gyrus (53, -65, 28), Posterior Cingulate/Precuneus (0, -62, 40) and Dorsal Medial Prefrontal Cortex (-16, 38, 40).

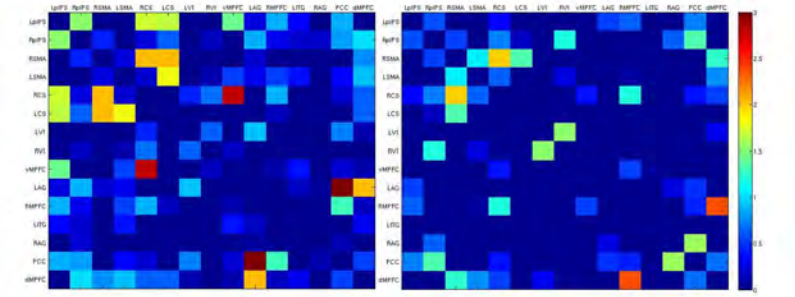

Fig 2. Z-score connectivity matrices obtained from correlation on healthy subjects and tumor patients.

DISCUSSION

Anatomical changes may complicate the recognition of networks in tumor patients especially in the presence of altered connectivity. However, several rs-networks were recognizable with ICA, thus providing an improved study specific node selection for functional connectivity. Connectivity comparisons show that in patients some connections are totally lost and other reveal weaker coupling compared to healthy subjects. For example, LpIPS has a weaker connection with RpIPS, RCS and vMPFC. In addition, especially connectivity of SMA to other SMN nodes seems to have reduced. As well, PCC node shows decreased connectivity in patients. These two nodes act as main hubs in their networks and thus could explain possible cognitive decline in tumor patients.

CONCLUSION

Based on the ICA results we conclude that various rs-networks are identifiable on tumor patients, although in some cases connectivity disruptions exist even far away from the lesions. Altered network locations due to anatomical changes and possible plasticity offer a challenge in node selection for connectivity analysis but prior recognition of important nodes based on ICA can improve the method. Further validation of chosen method with larger patient population is needed to study whether the location of a lesion in comparison to a specific network hub might have a higher impact on functional connectivity and if the decrease of overall connectivity in patients could be explained by the fact that connectivity of the important hubs is affected.

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