A Whole Brain Approach to Study Altered Functional Connectivity in Gliomas

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Introduction:

Gliomas are the most common primary brain tumours in adults. Gross total resection is associated with better outcome and prolonged survival (Kreth et al., 2013), nevertheless, the benefits of a larger neurosurgical resection need to be balanced against the risk of altering the quality of life of the patient by inflicting deficits in eloquent functions (Ghinda et al., 2018). The mapping of these areas is currently performed via intraoperative stimulation or by studying brain functional connectivity. One of the main limitation of these approaches lies in that they are mainly focused on specific brain functions such as motion and language, or brain networks, located in the perilesional area. However, it is a well know phenomenon that brain lesions can also alter the function of remote brain areas. Here we propose a method to identify at whole brain level altered as well as preserved functional networks without the need tumour location previous.

Methods:

Thirteen patients (8 males, age 59±19y) with newly diagnosed glioma (9 high grade; 4 low grade) were scanned before surgery with a Siemens 3T Biograph mMR scanner. The control group consists in 23 healthy subjects (13 males, age 40±11y). Both groups followed the same acquisition protocol, which included a T1-weighted (1mm isotropic), a T2-weighted Fluid Attenuated Inversion Recovery (FLAIR, 1mm isotropic), 15 minutes of resting state functional magnetic resonance imaging (rs-fMRI, echo planar imaging: MBfactor 2, TR/TE

1260/30ms, 3mm isotropic) and two spin echo images acquired with inverse readout directions.
For each patients FLAIR image hyperintensities were manually segmented at the aim of delineating the tumour extent. Each subject's rs-fMRI data underwent a standard pre-processing, which was performed with a combination of FMRIB Software Library (Smith et al., 2004) and Advanced Normalization Tools (Avants et al., 2011), and included slice timing, readout distortion and motion correction and non-linear coregistration to the asymmetric MNI 2009c atlas (Fonov et al., 2011) passing through the subject's T1 image. The control group pre-processed data were analysed by means of independent component analysis (ICA) in order to obtain reliable spatial maps of the main resting state networks (RSNs), using the group ICA of fMRI Toolbox as in (Allen et al., 2012). Exploiting the group-information guided ICA (GIG-ICA) (Du & Fan, 2013), the obtained spatial maps were used as guidance to compute individual specific independent components both in patients and in controls. Group RSNs components were manually selected according to (Allen et al., 2012) and masked (threshold: 3 standard deviation).
In order to identify affected RSNs, for each patient/control and each RSN, we then computed the cosine similarity measure (CSM) between the group and the individual map within the RSN group mask.

Results:

Figure 1 shows the CSM computed RSN by RSN for the control and glioma patient groups. RSNs are sorted on the basis of their reproducibility in the control group, estimated as a combination of minimum standard deviation and maximum median of the CSM.
Figure 2 illustrates a representative sagittal, coronal and axial slice of the obtained salience network (first row of Figure 1) at the control group level and for two different patients. From the figure, it is clear how CSM is a sensitive index in highlight differences in patients RSN spatial pattern, and how the presence of the tumour impacts this specific network not only in the peri-lesional area, but also at distance, which is in line with the current hodotopical approach to the study of the glioma impact on brain functioning.

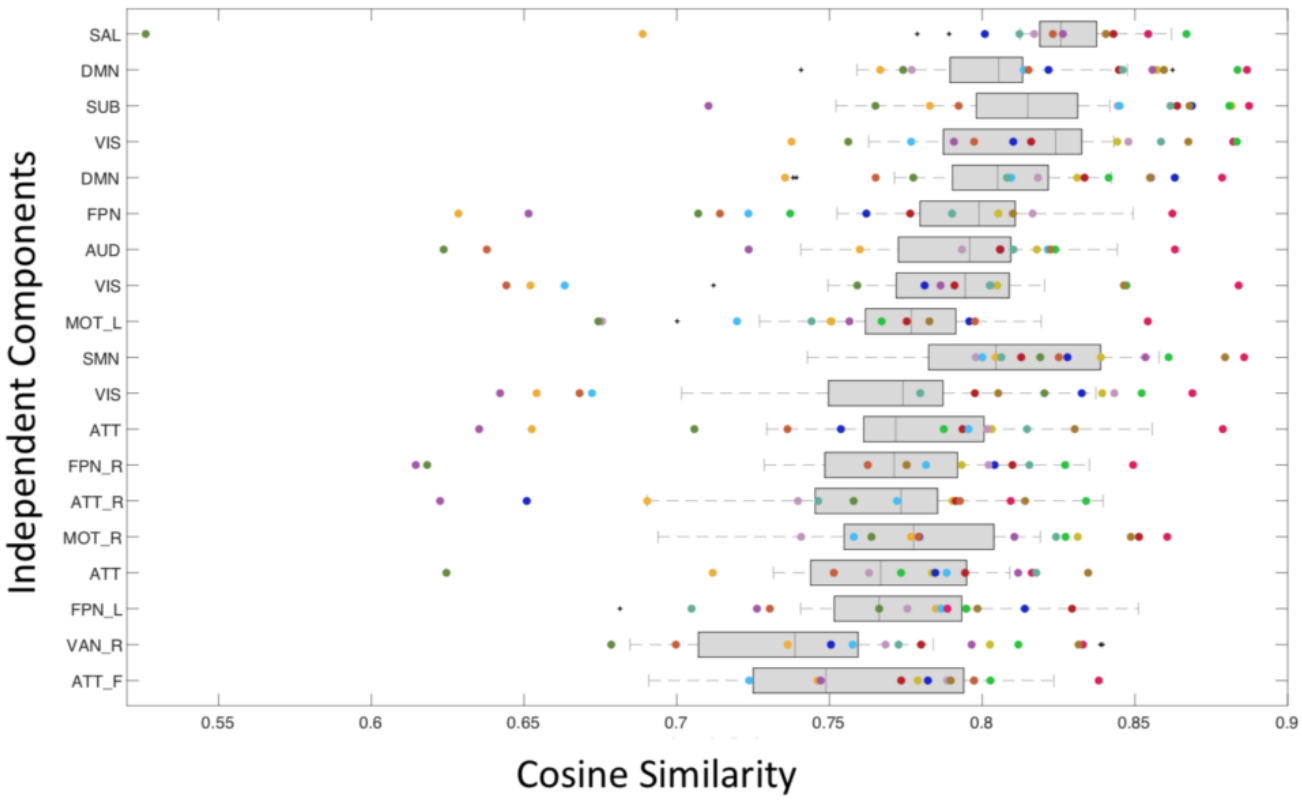

Figure1: Cosine similarity measure computed for each independent component representing a resting state network (on the y axis). Healthy controls results are reported as grey boxplot, whereas for each patient the cosine similarity is reported with a different colour dot.

Resting state networks are labelled as follows: SAL= salience network, DMN= default mode network (part), SUB= subcortical grey nuclei, VIS = visual network (part), AUD = auditory network, MOT_L = left motor network, MOT_R = right motor network, SMN = somatosensory network (part), ATT = dorsal attention network (part), ATT_R = left dorsal attention network (part), ATT_F = dorsal attention network (bilateral frontal nodes), FPN = fronto-parietal network (part), FPN_L = left fronto-parietal network, FPN_R = right fronto-parietal network, VAN_R = ventral attention network (part).

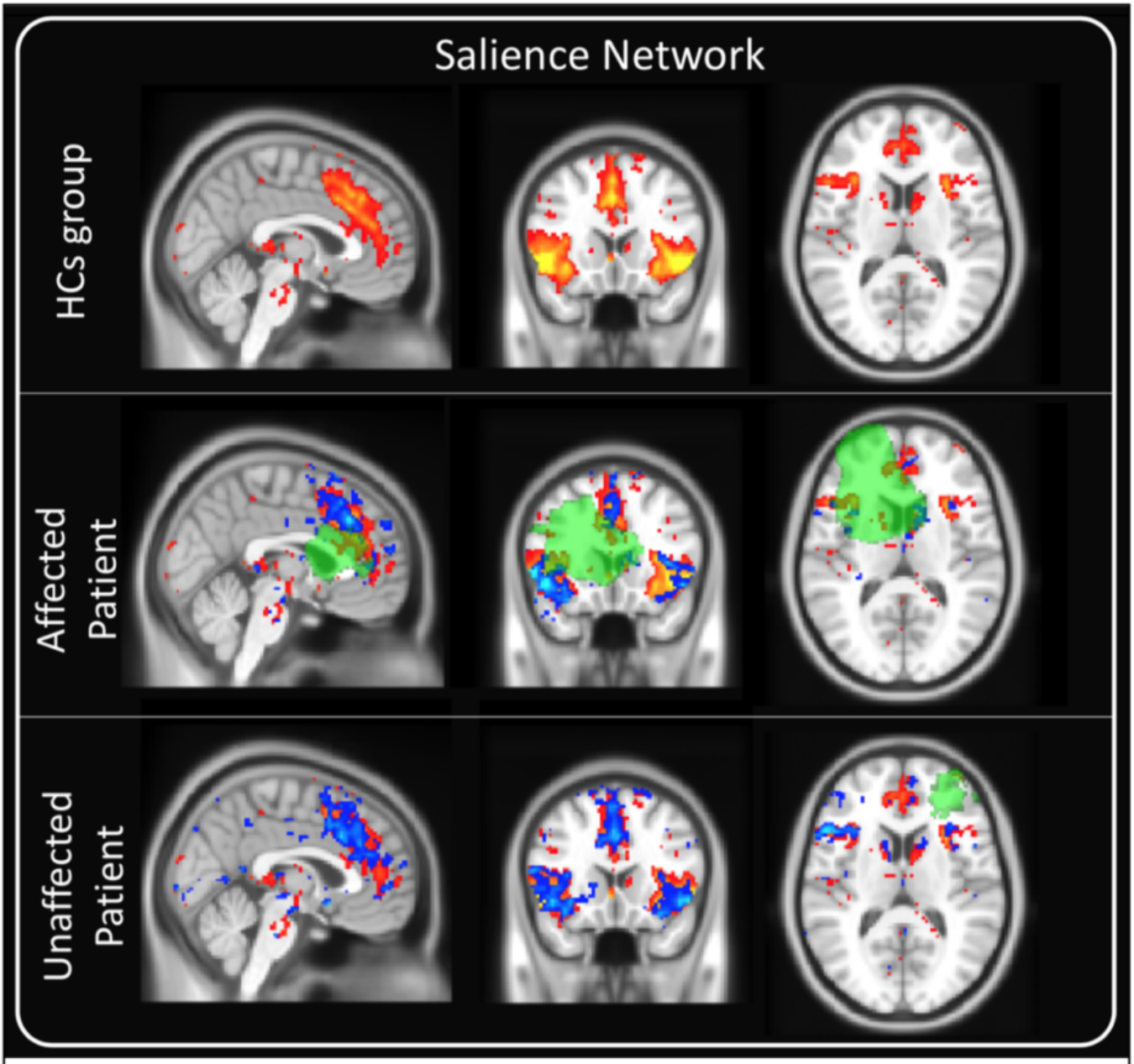

Figure 2: Sagittal, coronal and axial representative slices of the obtained Salience Network. In the first row the healthy controls group result (hot scale), in the second the same RSN map (blue scale) obtained for a patient where the network is highly altered even in areas far from the tumour (green), in the third the same RSN map (blue scale) obtained for a patient where the network is preserved (tumour in green).

Conclusions:

The proposed method revealed to be efficient in detecting alterations in glioma patients' resting state network and provides a valid approach in the study of functional connectivity at the whole brain level, instead of limiting the analysis on specific networks such as language network or default mode network.

Imaging Methods:

BOLD fMRI [2]

Modeling and Analysis Methods:

fMRI Connectivity and Network Modeling [1]

Keywords:

FUNCTIONAL MRI
Other - Glioma

[1|2]Indicates the priority used for review