

Spontaneous Low-Frequency BOLD Signal Fluctuations: Changes in Default Mode Network in Brain Diseased with Glioblastoma

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INTRODUCTION:

More than thirty years of brain imaging research has shown that brain is very active even in the absence of explicit external input or output [1]. Examining slow (<0.1 Hz) spontaneous fluctuations in the blood oxygen level dependent (BOLD) signal of functional magnetic resonance imaging (fMRI) has been demonstrated to allow the identification of functionally correlated networks at rest, the so-called resting state networks. Among those, the “default mode network (DMN)” as constituted by medial prefrontal, hippocampal, posterior cingulate and inferior parietal cortical regions has been associated with the processing of internally focused cognitive tasks. It has been demonstrated that neurological disorders such as Alzheimer’s disease may lead to disruption of the DMN [2]. However, it is not thoroughly examined how brain tumors and their associated treatment affect the integrity of the default network. Thus, in this pilot study quantitative change in the DMN were assessed in patients with glioblastoma (GB).

METHODS:

Patients: Four GB patients were scanned using a 3T Siemens MRI scanner with a 32-channel head coil after surgery.

Data Acquisition: Simultaneous BOLD sequence based on pulsed ASL sequence was used. It applied single-shot, gradient echo (GE) echo planar imaging (EPI) acquisition with a 64×64 matrix. Eight-slice images with 8mm thickness were acquired using the optimized TE and TR for BOLD (TR/TE=2000/19 ms, FOV = 220mm, 6/8 partial Fourier). Post-contrast (gadolinium-DTPA). All subjects were asked to stay in the resting state with open eyes. T1-weighted high-resolution three-dimensional images – MEMPRAGE - were acquired for anatomical details.

Data Analysis: The data processing consisted of a coregistration with MRMPRAGE using Freesurfer and SPM5 software packages, a motion correction and a connectivity analysis using custom software developed by Buckner’s Lab [1]. The connectivity analysis was based on an approach to extract the BOLD time course from a seed region - posterior cingulate (PCC) – and determine the temporal correlation between this extracted signal and the time course from all other brain voxels, creating a DMN map [3]. The z-score outputs were assessed bilaterally in the inferior parietal cortex (IPL), a region usually strongly correlated with the PCC-seed. Two isocontour threshold ROIs were defined, one on the hemisphere affected by the tumor (DMN_T) and one on the contralateral hemisphere (DMN_C).

RESULTS AND DISCUSSION:

The z-core connectivity maps overlaid on the corresponding structural images for one healthy subject and for two representative GB patients are shown in **Figure 1 a-d**. In general, it was possible to identify coherent BOLD DMN-activity in brain tumor patients in a similar pattern as demonstrated previously in healthy subjects (**Fig 1 a**). However, distinct asymmetry of the DMN was observed with a decreased connectivity of the IPL in tumor-affected hemisphere. This was the case when the tumor location regionally interfered with the DMN (**Fig 1 b**), but interestingly also for more remotely located tumors without direct contact to the region of measurement (**Fig 1 c and d**). As shown in **Table 1**, z-score values were reduced in a hemisphere diseased with GB compared to those in a contralateral hemisphere for three subjects. Only one exceptional case (patient ID #2) with a very small and remotely located GB (temporal pole) did not show affection of the DMN-symmetry.

CONCLUSION:

These preliminary findings suggest that the presence of a brain lesion, as induced by a GB and/or corresponding treatment may result in a disintegration of the resting state default mode network on the affected hemisphere. The network can show disruptions even in regions remote from the actual tumor location. The measurement of resting state connectivity in brain tumor patients by assessment of spontaneous low-frequency fluctuational BOLD signals may improve the understanding of impairment of brain functions associated with brain regions not directly affected by the tumor. Furthermore, the repeated assessment of the DMN in the course of brain tumor therapy may provide a valuable tool for the measuring treatment effects on brain functional parameters.

REFERENCES:

- [1] Buckner RL et al., Ann. N.Y. Acad. Sci. 1124: 1–38 (2008)
- [2] Sorg C, Drzezga AE et al., Proc Natl Acad Sci. 20;104(47):18760-5 (2007)
- [3] Fox MD et al., Nature 8:700-11 (2007)

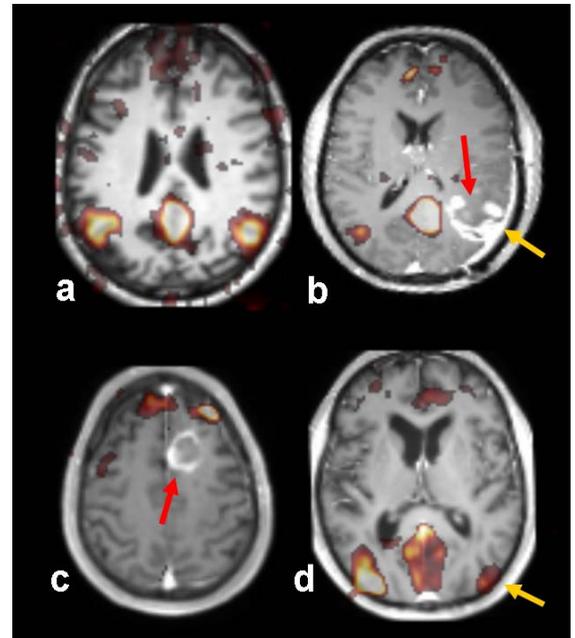


Fig 1. Top a): z-score connectivity maps overlaid on structural images for a healthy subject (**Left**) and **b)** a GB patient ID #3 (**Right**), showing DMN-disruption (yellow arrow) by tumor (red arrow) **Bottom: c)** z-score connectivity maps overlaid on post-contrast structural images for another patient ID #1, showing a tumor (**Left**) and **d)** distant DMN defect (**Right**)

Patient ID	DMN_T	DMN_C
1	0.74	0.995
2	1.20	1.12
3	~ 0	1.15
4	0.76	0.84

Table 1. z-score values in the hemisphere where tumor locates (DMN_T) and in the contralateral hemisphere (DMN_C) for all subjects.