System imbalance of activated external awareness yet deactivated internal awareness in the vegetative state detected by resting state fMRI

Jianghong He[1], Yi Zhang[1,2], Zhenyu Zhou[3], Ruxiang Xu[1], and Yijun Liu[4]

[1]*Department of Neurosurgery, Beijing Army General Hospital, Beijing 100700, China,* [2]*School of Life Science and Technology, Xidian University, Xi'an, Shanxi 710071, China,* [3]*GE Healthcare, Beijing 100176, China,* [4]*Department of Biomedical Engineering, Peking University, Beijing 100871, China*

Introduction

Disorders of consciousness (DOC) can be classified as the coma, the vegetative state (VS), and the minimally conscious state (MCS). Patients in VS after four weeks is defined as persistent VS (PVS), and the chances to regain awareness decline with the time spent in VS. VS patients have compromised awareness yet retained wakefulness. The mental status of VS is distinct from coma (no wakefulness, and no awareness) and MCS (wakefulness with minimal awareness). Differentiating VS from MCS has been a challenging task based on behavior observations. Diagnostic errors in classifying persons in MCS as being in VS ranged from 37% to 43% and can have adverse consequences for clinical treatment [1]. Blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI) is increasingly being recognized as a valuable tool to decipher the complexity of the underlying mental states in DOC. In particular, resting-state BOLD fMRI is simple yet very useful in understanding the baseline functionality and connectivity in non-communicating or disabled patients [2]. BOLD-fMRI studies reveal that the two components of the awareness system are anti-correlates, which are believed to be of functional relevance to wakefulness, awareness, and consciousness. The present study performed resting state fMRI in DOC patients matched with healthy subjects. The resting state fMRI data were explored in a data driven manner by using independent component analysis [3] and amplitude of low-frequency fluctuation (ALFF) analysis.

Material and method

A total of twenty patients with DOC and twenty normal control subjects participated in the study. Finally, twelve patients (8 male, 4 female; mean age: 44.7 ± 17.5 yrs), and eighteen healthy control subjects (12 male, 6 female; mean age: 41.2 ± 10.2 yrs) were included. The research protocol was approved by the Institutional Review Board at the Beijing Army General Hospital and informed consent was obtained from their legal guardians. The DOC patients were evaluated by experienced raters using the CRS-R tool. The assessment explores the various sensory and cognitive aspects including auditory, visual, verbal and motor functions as well as communication and arousal level with the total score ranging from 0 (worst) to 23 (best).

MRI was performed on a GE Signa HDi 3.0T scanner. fMRI was acquired using an T2* weighted echo-planar imaging sequence sensitive to the BOLD contrast with the repetition time = 2000 ms, echo time = 30 ms, slice thickness = 4.0 mm with the interslice gap of 0.6 mm, field of view = 220 x 220 mm^2, matrix size = 64 x 64, and flip angle = 90° . The total scan time was 8 minutes, containing 240 time points. The preprocessed data were then arranged into Group ICA of the fMRI Toolbox (GIFT, http://icatb.sourceforge.net/). Using the Informax ICA algorithm, the number of independent components (ICs) was separated by Group ICA, which was estimated to be 30.The amplitude of low-frequency fluctuation (ALFF) analysis was carried out using the REST software to define the ROIs.In order to assess the association between changes in ALFF of brain activity and clinical measurements, we measured the correlation between the mean activation of each ROI and the clinical measurements.

Results and Discussion

In normal control group, the structures of DMN were observed with activation during the resting state, including MPFC, PCC and bilateral IPL. By contrast, the activation of VS patients exhibited a distinct pattern of DMN both in spatial and strength. In addition, middle occipital cortex and areas in cerebral also exhibited decreased activation. Compared with the control group, our data shows that the VS patients were observed with an increasing ALFF in the insula (Brodmann Area, BA 13), lingual gyrus (BA 17, 18, 19), paracentral (BA 5, 6) and supplementary motor area (SMA)($P < 0.05$, FDR correct; Fig. 1). ALFF analysis also showed that DOC patients of VS in the resting state were observed with a decreasing trend in the regions including the medial PFC (MPFC, BA 10), anterior cingulate cortex (ACC; BA 24, 32), posterior cingulate cortex (PCC; BA 29, 30), thalamus, orbitofrontal cortex (OFC), parahippocampus (PHIPP; BA 30, 35, 36), caudate, cuneus (BA 18, 19), inferior parietal lobule (IPL; BA 40), and precuneus ($P < 0.05$, FDR correct;).

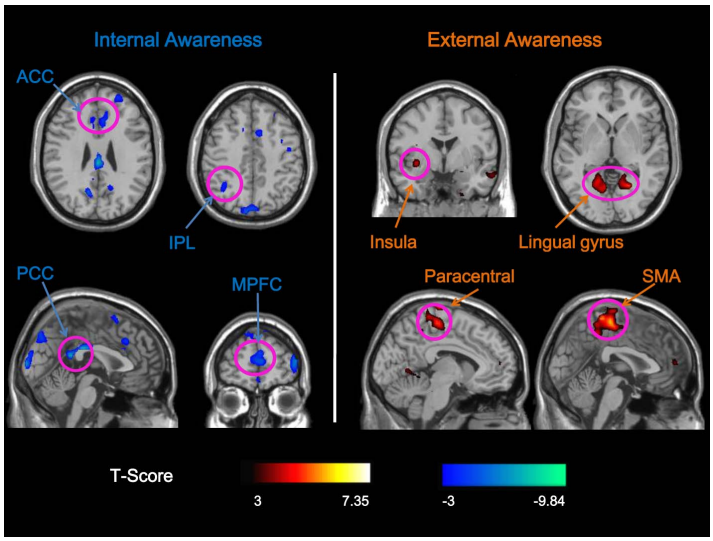

Fig.1 Areas with altered activity in ALFF of the VS patients compared to controls. An increasing trend was seen in the insula, lingual gyrus, SMA, and paracentral while a decreasing trend in the regions including the MPFC, ACC, PCC, thalamus, and IPL.

References

[1] K. Andrews. British Medical Journal 1996, 313: 13-16. [2] B.B. Biswal. Neuroimage 2012, 62: 938-944. [3] C.F. Beckmann, Philosophical Transactions of the Royal Society B: Biological Sciences 2005, 360: 1001-1013.