Task Performance Classified Resting-State Functional Connectivity Analysis for Blast-Related Mild Traumatic Brain Injury

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Introduction

Abnormality of brain functions impacts not only task related brain activity but brain functional connectivity. More and more recent fMRI studies have established relationships between resting-state functional connectivity and brain activation during the performance of a cognitive task. Some studies compared brain intrinsic connectivity with or without task performance [1]. Some correlated connectivity alterations with task performance variables [2]. On the other hand, due to the heterogeneous nature of mild Traumatic Brain Injury (mTBI), further classification may help to identify subpopulations of patients in order to better target their treatments. Therefore, in this study, we applied the results of task performance analysis to classify mTBI subjects into different groups and then performed further resting-state functional connectivity analysis among mTBI subjects and between mTBI subjects and healthy controls.

Methods

81 clinically categorized mTBI patients from USA military personnel during post-acute phase (> 2 months) and 22 age-matched healthy controls (military members who had not been previously deployed) were enrolled.

The MR examinations were performed at the National Intrepid Center of Excellence (NICoE), using a GE 3T whole body MR Scanner (GE750 Systems, GE Healthcare, Milwaukee, WI) equipped with a 32-channel phased array head coil. A T1-weighted high-resolution anatomical image was acquired using the GE BRAVO sequence (TR/TE 6.7/2.5ms, FOV 240x240mm^2, in sagittal plane) in order to register fMRI data to MNI standard space. Subjects then were asked to lie still in the scanner at rest and close their eyes. 180 volume fMRI images were acquired in sagittal plane with the following parameters TR/TE 2000/25ms, FOV 240x240mm^2, matrix 64x64x40, slice thickness 4mm. Following this, a 215 volume Go-NoGo paradigm with word/color Stroop stimuli was acquired using the same imaging parameters as resting-state fMRI scan. Each Stimulus consisted of the word of "Red", "Green" or "Blue" displayed in red, green, or blue color. Subjects were asked to press left or right paddle button when seeing word "Red" or "Green", and stop when seeing word "Blue". The task consisted of 124 trials with about 20% (25) NoGo stimuli. Intertrial intervals ranged from 1.6 to 2.2 seconds.

Subject responses to the Go-NoGo task were recorded and sorted by NoGo errors (word "Blue" was presented and a paddle button was pressed). 21 mTBI subjects with 3 or more NoGo errors (mean 6.52, standard deviation 4.73) were selected to form the mTBI group with poor performance [P]. 21 mTBI subjects randomly selected from 36 mTBI subjects with no NoGo errors and total response correctness greater than 109 trials were selected to form the mTBI group with good performance [G]. 18 healthy controls (one with 2 NoGo errors and three with 1 NoGo error, 15 have no NoGo errors) were selected to form the control group [C], 4 controls were excluded from analysis due to having more than 2 NoGo errors.

Resting-state fMRI data corresponding to task performance classified poor [P], good [G] performing mTBI and healthy control [C] groups were then compared as [P] vs. [G], [P] vs. [C] and [G] vs. [C]. MELODIC (FSL, Oxford) group independent component analysis (GICA) tool was employed to decompose temporal concatenated group data with automatic dimensionality estimation after standard FSL preprocessing: first 3 volumes removed, high-pass filter cutoff 100s and spatial smoothing kernel FWHM 6mm. 1 subject was removed from [P] due to only 163 volumes acquired, thus 20 subjects were included in this group. Dual regression analysis (FSL) was then performed on all GICA components in 3 pairs. For each resting-state network, differences between groups were tested using threshold-free cluster enhancement (TFCE), non-parametric permutation testing (5,000 permutations, randomize, FSL) with a thresholded component-specific mask (IC map thresholded by $p > 0.5$). Family-wise error corrected voxels were then thresholded at $p < 0.05$.

Results and discussions

37, 35 and 44 independent components (IC) were identified from [P] vs. [G], [P] vs. [C] and [G] vs. [C], respectively. Of them, 3, 2 and 1 resting-state networks showed the regions of significant differences (Fig. 1, in green color), respectively.

For mTBI poor group [P] vs. mTBI good group [G], (a) is midline cortical-subcortical network which is predominantly involved in error processing [3]. Significant decreases for [P] than [G] indicated the reduced error processing capabilities of [P]. (b) is right fronto-parietal network which is related to attentional monitoring for stop signals [3] and reflected the fact that subjects in [P] failed to inhibit their button presses during stop signal trials. (c) is part of language network. [P] showed less connectivity on word reading and interpreting ability than [G].

For mTBI poor group [P] vs. control group [C], (d) is bilateral striatum network which is associated with response inhibition [4]. [P] showed decreased connectivity in left thalamus/parahippocampal. (e) showed large connectivity reduction area in midline cortical-subcortical network, which indicated that [P] lost significant capability for error processing than healthy controls.

mTBI good group [G] vs. control group [C] had almost no connectivity differences except some scattered points in brain prefrontal area seeing in (f), which may reflected compensatory increases of local efficiency after brain injury [5]. This finding also implied some mTBI patients may fully recovered from injury.

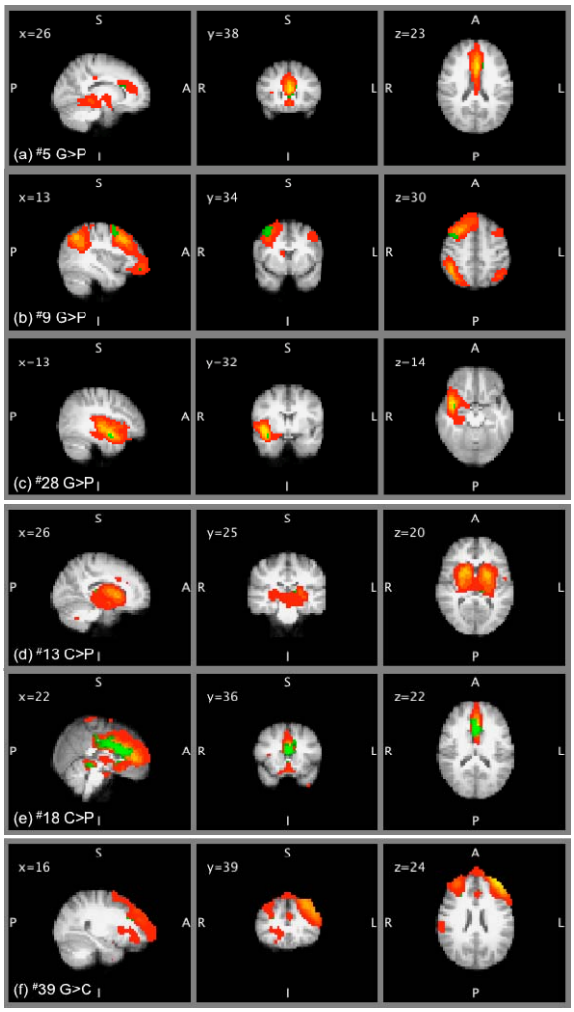

Figure 1, IC maps (warm color) and connectivity difference regions (cold color).

Conclusions

This study demonstrated that task performance could be used for classifying resting-state fMRI data for mTBI. The results revealed great differences in intrinsic fluctuation among mTBI, and the brain dysfunction regions matched the current findings [3, 4, 5]. The novel approach may apply for studies with other cognitive tasks, and for other brain disorders.

References: [1] Calhoun et. al., HBM 2008; 29:828-838. [2] Caeyenberghs et. al., Brain 2012; 135(4):1293-1307. [3] Zhang et. al., HBM 2012; 33:89-104; [4] Zandbelt et. al., PLoS ONE 2010; 5(11); [5] Zhou et. al., ISMRM 20 (2012), 374.