Functional connectivity after fronto-occipital impact mild traumatic brain injury

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Background. More than 90% of all traumatic brain injuries (TBI) are considered mild (MTBI). Up to 50% of MTBI patients develop persistent post-concussive syndrome. Abnormal neuropsychological test results after MTBI usually show memory deficits, impairments in the rate of information processing, and attentional deficits. However, computed tomographic (CT) and conventional magnetic resonance (MR) imaging results of MTBI patients are typically normal: CT abnormalities are visible in only 6-10% MTBI patients; MRI abnormalities are more easily detected, but demonstrate only a weak correlation with neuropsychological tests during the acute period.

Objective. We hypothesize that post-traumatic complaints are associated with modified brain functional connectivity rather than structural lesions per se. It has been shown that the most frequently cognitive deficits observed after MTBI are related to verbal and visual memory, disturbed planning, problem solving, impaired information processing, and attention [1, 2]. This is indicative of damage to frontal cortical and subcortical regions. Hence we assumed that the mechanism of head injury in fronto-occipital impacts may be the most advantageous in analyzing MTBI abnormalities. Therefore the objective of this study is to evaluate the alterations in the whole-brain functional connectivity after fronto-occipital impact MTBI and correlate the degree of functional disruption to cognitive deficits.

Methods. 22 acute MTBI patients (age 18-58 with a mean age of 40, 11 males) were studied within 2-26 days after injury (mean time of 12 days). To select only patients with fronto-occipital injury we used at least one of the following indications as the inclusion criterion: frontal/occipital impact mechanism, extracranial swelling in frontal/occipital part, facial fracture, intracranial CT abnormalities in frontal/occipital lobes. 22 healthy controls matched by age, gender, and educational level were also recruited for comparison.

All participants were scanned at resting state in a 3.0 T system (Magneton TRIO, Siemens) using a GE EPI sequence (TE/TR = 30/1350 ms, flip angle = 70º, 27 slices, slice thickness 3.5 mm with slice gap = 0.7 mm, matrix size 64 × 64, voxel size = 3.5 x 3.5 x 3.5 mm, 265 volumes, bandwidth = 1906 Hz/pixel). The first 5 volumes were discarded to allow for T1 saturation effects. All remaining images were coregistered to each other and normalized to the EPI template. No spatial smoothing was performed. To reduce low-frequency drift and high-frequency fluctuations, the fMRI data was temporally band-pass filtered (0.01 – 0.08 Hz).

Whole-brain functional connectivity was evaluated by means of partial correlation coefficients (z-value) for all possible pairs of regions parcellated using the AAL template [3]. Functional connection between a pair of regions was considered as significantly altered between 2 groups if: (1) z-value was significantly different from zero at least in one group at P<0.05 (one-sample two-tailed t-test, FDR corrected) AND (2) z-value was significantly different between the two groups at P<0.05 (two-sample two-tailed t-test) [4].

Results. In total, 15 connections were significantly different between MTBI patients and controls. MTBI patients showed significantly decreased z-values in 9 functional connections and increased z-values in 6 other connections compared to the controls.

![Image](Figure 1. Normalized numbers of decreased (A) and increased (B) functional connections related to each brain area.)

The global distribution of altered functional connections between nine brain areas is shown on Fig. 1. As all brain areas include different number of regions, the number of the altered connections related to each of the nine brain areas was then normalized by dividing the number of all possible connections related to this area. This analysis shows that the decreased connections are involved with five brain areas. The majority of decreased connections belong to prefrontal and (to a lesser degree) to temporal and parietal areas. The increased functional links in MTBI are more evenly distributed throughout the brain and not restrained to one specific area. Finally we found the relation between the strength of decreased in MBA functional connection within prefrontal area (orbital part of superior frontal gyrus and gyrus rectus) and information processing speed decreased in MTBI. In the healthy control group the connectivity strength (assessed as z-value of partial correlation coefficient) between these regions is significantly positively correlated (r = 0.55; P<0.05) with information processing speed (assessed as the reaction time in the Stroop test). However this positive correlation is disturbed in MTBI group (Fig. 2).

![Image](Figure 2. Correlation between strength of functional connection between superior frontal gyrus (orbital part) and gyrus rectus, and reaction time score (r=0.55, p < 0.05). Controls are shown in blue, MTBI patients in red.)

Conclusion. We used the resting state fMRI to relate the cognitive deficits occurring after fronto-occipital impact MTBI to the disruptions in functional connectivity. We found the disintegration of prefrontal, temporal and parietal regions in resting-state networks of MTBI patients and showed that the disconnection between prefrontal regions underlies the decline in the rate of information processing. Further investigation should be focused on the correlation between the degree of functional disruption and the other cognitive deficits observed after MTBI.