

Thalamic gray matter volume reduction in mild traumatic brain injury

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Detailed information on the pathology that evolves after brain injury is incomplete. In animal models of brain trauma, cortical impact causes delayed neuronal changes in the thalamus (1, 2). There is some evidence in models of human TBI that neuronal loss occurs within the thalamus, but very few systematic studies of such loss have been undertaken (3, 4). Based on these recent reports we hypothesized that mild traumatic brain injury is associated with subtle gray matter reduction in thalamic nuclei that could be detected on high resolution T1-weighted imaging.

Methods

We have examined 29 consecutive TBI patients, 10 women, 19 men; aged 33.9 ± 10.3 years (mean \pm standard deviation) and 18 healthy volunteers (9 women, 9 men; 33.9 ± 9.5 years old). All patients had a mild head injury that caused a relatively short (<30 min) period of loss of consciousness. Their initial Glasgow Coma Scale was 13-15. Patients were screened by medical history and physical examination to exclude alcohol abuse, cardiovascular risk factors, hypertension, and diabetes mellitus. MRI were obtained on a 1.5 Siemens Vision using a comprehensive protocol. Clinical MRI findings were unremarkable for 25/29 patients, three had a contusion, one a subdural hematoma. Neither foci of microhemorrhage nor lesions suggestive of diffuse axonal injury were seen on any images. MPRAGE images (TR/TE=9.7/4 ms; FOV, 210×210 mm; 1.5 mm thick; matrix 256×256; FA, 15°, **Fig.1**) were used for thalamic volumetry.

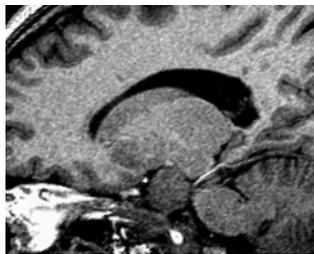


Figure 1

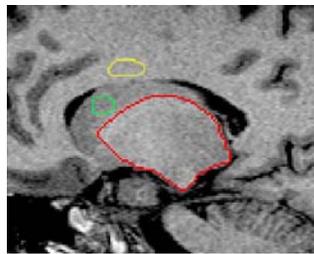


Figure 2

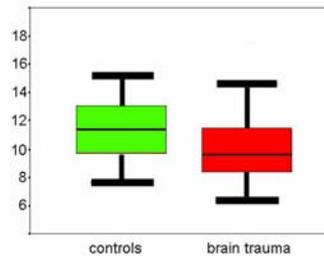


Figure 3

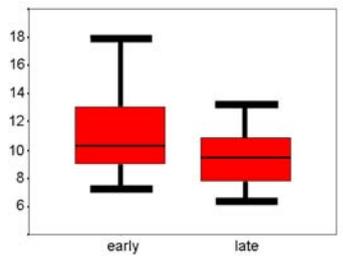


Figure 4

Thalamic volume was estimated using a technique that corrects for partial volume effect. The method requires the human observer to: 1) draw an over-inclusive region R (red outline on **Fig.2**) on all slices containing the thalamus; 2) outline six samples of caudate nucleus (green) and corpus callosum (yellow). Signal intensity of caudate and corpus callosum samples were averaged, yielding “pure” gray matter G and pure white matter W . Averaging serves to improve reproducibility and to account for image nonuniformities. For each voxel within the total thalamic region, the signal intensity S was converted to the quantity $f = (W-S)/(W-G)$, that reflects voxel’s gray matter content (partial volume). Thalamic gray matter volume was obtained by integrating f after applying the 20% and 80% cutoffs to reduce the sensitivity of the method to image noise.

Results

There was a good agreement between thalamic gray matter volume measured by two independent observers, with interclass correlation $\kappa=0.88$ (95% confidence interval 0.67-0.96). Thalamic gray matter in mild TBI ($10.3\text{ml} \pm 2.7\text{ml}$) was lower than in normal controls (11.5 ± 2.2), $T=1.63$, $df=42.1$, 1-tailed t-test, $p=0.046$ (**Fig. 3**). To investigate whether these changes are a transient post-traumatic phenomenon, the TBI patients were stratified into two groups based on the time interval between MRI and the date of injury (**Fig.4**). There was a trend ($t=1.49$, $df=25.2$, t-test $p=0.07$) for thalamic volume to be smaller (average difference 1.4 ml) in 8 patients examined after 3.7 ± 4.3 years after injury as compared with 21 patients who underwent MRI within 6.2 ± 10.6 days from the traumatic incident. This trend persisted after covarying for subject’s age and gender. (ANCOVA, $F=2.37$, $p=0.14$).

Discussion

Our results suggest that high-resolution structural T1-weighted imaging combined with partial volume correcting method is capable of measuring the volume changes in thalamic nuclei among the patients with mild brain injury. This reduction appears to be occurring at least several months after the time of injury. Reduced volume of thalamic gray matter could become a radiological marker of thalamic involvement and may correlate with the complex post-concussion syndrome in patients with mild traumatic brain injury.

References

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