Behavioral correlates of subtle anatomical abnormalities following traumatic brain injury


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INTRODUCTION

Neurocognitive assessment

Traumatic brain injury (TBI) patients with chronic cognitive deficits often fail to present abnormalities on standard magnetic resonance images (MRI). We developed novel quantitative imaging methods that are sensitive to subtle structural brain anomalies. We used these methods to detect and characterize cortical and white matter abnormalities in a severe TBI patient whose neuroradiological examination did not reveal any significant brain damage despite chronic problems in cognition and emotion.

METHODS

Case presentation. A 34 year old male suffered TBI in a motor vehicle accident. He was in a coma for 15 days, with a Glasgow Coma Score (GCS) of 3 and post-traumatic amnesia (PTA) lasting 23 days. Five years post-injury, he remains unable to work due to severe cognitive and emotional impairments.

Neuroimaging. High resolution T1-weighted structural MRI and diffusion tensor imaging (DTI) scans were acquired from the patient (two sessions) and 43 age-matched controls. The cortical surface was extracted and cortical thickness computed from T1 images (Figure 1) using FreeSurfer [1]. Fractional anisotropy (FA) and mean diffusivity (MD) were computed on the cortical surface and pericortical white matter [2].

Morphometric analysis. Cortical abnormalities were assessed using surface-based morphometry (SBM), subcortical white matter integrity was assessed using tract-based quantification of DTI data, and the structural integrity of the corpus callosum was analyzed using an automated segmentation and partitioning procedure [3]. The combined Fisher test, corrected for covariations between interdependent measurements [4] was used to assess jointly the abnormalities evident in co-localized multimodal data.

RESULTS

Surface-based morphometry (SBM) of cortical abnormalities

Regional cortical abnormalities were assessed by comparing regional cortical thickness, cortical diffusivity, and pericortical white matter anisotropy (2 mm below the gray/white boundary) and diffusivity between the patient and the mean values for the control group [5].

Figure 2. Widespread cortical thinning (A), increased cortical gray matter diffusivity (B), and pericortical white matter abnormalities (reduced anisotropy and increased diffusivity, C) were found in the two hemispheres. Combined assessment of the co-localized abnormalities evident in individual tissue metrics revealed extensive structural abnormalities that were most pronounced in frontal and occipital regions (D), and which replicated in a second imaging session (E).

Figure 3. Fractional anisotropy was quantified along major tracts using probabilistic fiber maps in standard (MNI) space [5]. Reduced white matter integrity was evident in a number of fiber tracts as lower mean FA values (scaled from 0 to 10) for the patient (red diamonds for two sessions) compared with controls (histograms).

Structural abnormalities in the Corpus Callosum

Figure 4. The structural properties of corpus were assessed using T1 anatomical images (left) and DTI scans (middle, red indicates medio-lateral orientation of transcallosal fibers). Abnormalities in the isthmus and splenium were evident on the FA map, but not T1 images (right).

Figure 5. The corpus callosum was extracted from segmented white matter images from T1 scans, and partitioned into seven compartments following Wittelson’s scheme [6] (left). Directional information from DTI was used to exclude the fornix and the cingulum bundle. Callosal abnormalities were evident in reduction in volumes of the genu and splenium, thinning of the isthmus, lower anisotropy and increased diffusivity in all compartments.

Neurocognitive assessment

Neuropsychological testing. Standardized tests showed severe cognitive impairment 3 years post-injury. Performance was in the 4th percentile on digit span test and in the 1st percentile for the California verbal Learning Test. Visual reproduction and most subtests of the Delis-Kaplan Executive Function System. There was no evidence of malingering. His everyday functioning remained severely impaired.

Computerized neurocognitive assessment. A TBI test battery developed at VANCiCS Martinez was administered to the patient and seven controls. Perceptual and motor processing speed, attention, executive function and visual interhemispheric integration were assessed. Task difficulty was adaptively adjusted to patient performance.

• Finger tapping, visual and auditory simple reaction time
• Feature conjunction, modified Paced Auditory Serial Addition Test (PASAT)
• Visual field comparison

Summary of computerized test findings:

• Abnormal fatigability and unstable performance, assessed by the effect of time-on-task and within task variability
• Motor slowing, assessed by finger tapping rate
• Reduced processing speed with increasing task difficulty
• Increased distractibility in the feature conjunction task
• Executive control impairment, assessed by the paced serial addition task (Figure 6)
• Impaired visual field comparison (Figure 7)

Figure 6. Paced serial addition task. Subjects added the last two in a continuously presented series of digits (1-9). Task difficulty adjusted by gradually increasing the presentation rate. Minimum interstimulus interval reached was below 2 seconds for controls, while the patient was severely impaired even when only two digits (1-2) were used.

Figure 7. Visual field comparison test. Subjects compared two briefly presented letters on opposite hemifields (inlay). Minimum exposure duration necessary for successful comparison was assessed using an adaptive staircase procedure. The patient needed a significantly longer duration than controls.

CONCLUSIONS

The structural alterations found in the cortex, white matter tracts and the corpus callosum, which were not evident on the patient’s neuroradiological examinations, adhere to the typical distribution TBI-related damage and can help to explain his chronic impairments. The frontal and basal distribution of the cortical abnormalities are consistent with the severe cognitive and emotional deficits commonly found in TBI. Perceptual and cognitive slowing is consistent with the extensive white matter abnormalities along major tracts. The patient’s poor performance on the visual field comparison task may reflect damage to the occipital cortex and splenium of the corpus callosum which would impair the integration of visual input from the two hemifields.

References