Computer-aided detection of slight volume loss can be used as a marker for brain pathology after mild traumatic brain injury

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Authors: R. Raininko\textsuperscript{1}, M. Lannsjö\textsuperscript{2}, M. Bustamante\textsuperscript{1}, R. Strand\textsuperscript{1}, J. Borg\textsuperscript{3}; \textsuperscript{1}Uppsala/SE, \textsuperscript{2}Uppsala/Gävle/SE, \textsuperscript{3}Stockholm/SE
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Purpose

There are many earlier radiological studies on traumatic brain injuries but they have most often included patients with different injury severity and the numbers of the patients with mild traumatic brain injury have remained low. A number of patients, up to 44% at 3 months after the trauma [1], have persistent symptoms after mild traumatic brain injury but it has been difficult to demonstrate morphological changes in this patient group.

We have explored brain pathology after mild traumatic brain injury by repeated MR and clinical examinations.
Methods and Materials

Patients: Twenty patients with mild traumatic brain injury presenting Glasgow Coma Scale 14-15 were recruited in the project and examined with MRI at 2-3 days after the injury. The second MRI and clinical examination were made 3-7 months later (median 4 months). One patient refused the second MRI, and the final material comprised of 19 patients, aged 17 to 63 years (median 28 years), 12 of the patients were females.

Methods: Conventional T1- and T2-weighted sequences including FLAIR sequences, a susceptibility-weighted gradient echo sequence, an SWI sequence and a diffusion-weighted sequence were used. All images were visually interpreted by one experienced radiologist.

In addition, the brain volume change was examined in each patient in T1-weighted 3D series using a computer-aided volume comparison method developed from already existing ideas on voxel-based morphometry [2]. It works by registering the first MRI of the patient to the second MRI using affine transformations, i.e. transformations that preserve straight lines and ratios of distances between points lying on a straight line. Once the two volumes are properly aligned, the program subtracts the first MRI (assumed to be the fixed-volume, or base) from the volume created by the registration. The result is another volume that indicates which voxels have changed the most according to the subtraction values. In coregistration of the two examinations, the reference points were located in the brain, not in the skull.

Clinical outcome was assessed by the Rivermead Post-concussion Symptoms Questionnaire (RPQ) [3], Rivermead Head Injury Follow-Up Questionnaire (RHIFUQ) [4], Hospital Anxiety and Depression Scale (HADS) [5], and Glasgow Outcome Scale Extended (GOSE) [6].
Results

The first MRI revealed pathology related to a recent trauma in one patient. His left hippocampus was oedematous with an increased T2 signal intensity (Fig. 1a-b) and mixed, partly increased and partly decreased, diffusion.

Haemorrhages were not detected in any of the patients.

The second MR examination showed volume loss in four patients (21%). It was visually detected in one patient and by the computer-aided method in three additional patients.

The only subject with visually detectable changes on the second MRI was the patient with the hippocampal injury. That hippocampus had shrunk and showed a high T2 signal intensity (Fig. 1c) and high diffusion.

Mild focal substance loss only revealed by the computer-aided volume comparison:

- Patient 1: Loss of parenchyma was localized in the corpus callosum around the roof of the left lateral ventricle (Fig. 2).
- Patient 2: Some gyri in the left lower parietal lobe showed substance loss (Fig. 3).
- Patient 3: A slight focal, but bilateral, sulcal widening between the corpus callosum and the posterior cingulum was found (Fig. 4).

In 14 patients, the computer-aided method did not detect any loss of substance.

In two cases, the co-registration of the two examinations was suboptimal and the results could not be interpreted. One of these two patients was the patient with the hippocampal injury and visible substance loss described above.

Clinical outcome: In the second examination, seven patients (37%) reported symptoms in RPQ, five (26%) reported changes in activity and participation according to RHIFUQ, five (26%) reported some anxiety and one (5%) mild depression in HADS. Fifteen patients reported the upper level of good recovery (GOSE 8) and four patients reported the lower level of good recovery (GOSE 7).

Relationship of the pathological MR findings and clinical outcome:
The patient with the visible hippocampus injury reported four symptoms (dizziness, nausea, fatigue and poor memory) in the first RPQ. In the second examination he only reported one symptom (fatigue) but a change in two out of ten items regarding activity and participation according to RHIFUQ.

The patients with a loss of parenchyma in computer-aided volume comparison:

- Patient 1 reported eight symptoms (headaches, nausea, sleep disturbance, fatigue, irritability, frustration, poor memory and longer to think) in the first RPQ and one symptom (headache) at follow-up.

- Patient 2 reported 13 symptoms (headache, dizziness, nausea, noise sensitivity, sleep disturbance, fatigue, irritability, depression, frustration, poor memory, poor concentration, longer to think and restlessness) in the first RPQ and 6 symptoms (headache, noise sensitivity, sleep disturbance, irritability, poor memory and double vision) at follow-up.

- Patient 3 reported 6 symptoms (headache, dizziness, nausea, fatigue, irritability and depression) in the first RPQ but no remaining symptoms at follow-up.

None of these three patients reported any anxiety or depression according to HADS at follow-up, nor any changes according to RHIFUQ.

All four patients reached the upper level of good recovery according to GOSE (i.e. score 8).
**Fig. 1:** Patient with hippocampal injury. A,B. In the first examination, the left hippocampus (arrow) is oedematous: it is enlarged and shows high T2 signal intensity. C. In the second examination, the left hippocampus is shrunken and has a high T2 signal intensity. All images with a FLAIR sequence.

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**Fig. 2:** Volume loss in the corpus callosum demonstrated by the computer-aided volume comparison method. Volume loss is marked by red colour in the roof of the left lateral ventricle. A. Axial image. B. Sagittal image.

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**Fig. 3:** Volume loss in left parietal gyri. A. Axial image. B. Coronal image.

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**Fig. 4:** Slight focal widening between the corpus callosum and the posterior cingulum. A. Axial image. B. Sagittal image.

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Conclusion

The times for the early and late MRI were chosen taking into account results of previous studies and clinical experience. The first time point, i.e. on days two or three post injury, was considered optimal in order to detect any oedema or haemorrhage, which may not be visible at the day of injury but may evolve during the initial days post injury and also may wear off within one week. The late time point, i.e. at three months or longer post injury, would allow for atrophy to develop and be visualised. We did not found any hemorrhages and oedematous changes with diffusion disturbance were only detected in one case but substance loss could be demonstrated in 21% 3-7 months after the trauma.

The software used in volume comparisons is new and under further development. The software results might in some cases have been biased by the registration process, especially in cases where the patient's position changed significantly from one MRI to the other. Therefore, the volume comparison failed in two patients in our study. However, we believe that using of reference points in the brain in coregistration may give better results than using of reference points in the skull bone because the brain may have a little different position in two examinations.

This is an exploratory study with a small material but loss of brain volume after mild traumatic brain injury may be a feasible marker of traumatic brain pathology. Volume loss may be very slight and only be detected by computer-aided methods.
References


Personal Information

Raili Raininko MD PhD, Department of Radiology, University of Uppsala, Sweden; Raili.Raininko@radiol.uu.se

Marianne Lannsjö, MD PhD, Department of Neuroscience/ Rehabilitation Medicine, University of Uppsala, Uppsala, Sweden and Center for Research and Development, Uppsala University/County Council of Gävleborg, Gävle, Sweden; marianne.lannsjo@lg.se

Mariana Bustamante MSc, Centre for Image Analysis, University of Uppsala, Uppsala, Sweden, currently PhD Student, Division of Cardiovascular Medicine, Department of Medical and Health Sciences, Linköping University, Linköping, Sweden; mariana.bustamante@liu.se

Robin Strand PhD, Centre for Image Analysis, University of Uppsala, Uppsala, Sweden; robin@cba.uu.se

Jörgen Borg MD PhD, Department of Clinical Sciences/ Rehabilitation Medicine, Karolinska Institutet, Danderyd Hospital, Stockholm, Sweden; jorgen.borg@ki.se