Dynamic evolution of atrophy after traumatic brain injury.

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100 word synopsis of abstract:

Traumatic brain injury (TBI) is a major cause of morbidity and mortality worldwide. It is clear that much of the sequelae are not just a direct consequence of the acute event but represent a dynamic process with changes continuing to occur months to years after the precipitating injury. In this study, longitudinal changes in brain structures known to be important after TBI are presented. The differential effects of volume change are consistent with progressive but selective damaging effects of TBI indicating that individual regions have different vulnerabilities to the effects of injury.

Introduction: It is clear that many of the sequelae of Traumatic Brain Injury (TBI) are not just a direct consequence of the acute event, but represent a dynamic process, with changes occurring many years after the event. Such ongoing pathophysiology raises the hope for effective late treatments. However, a rational definition of the therapeutic window critically depends on being able to define the temporal pattern of such progression. Here we use T1-weighted magnetic resonance (MR) imaging to investigate the temporal changes in regional volumes after TBI.

Methods: Twelve patients (median age 24 years, range 17 to 59) who had sustained moderate to severe TBI requiring intensive care, underwent serial MR imaging on between three and five occasions. All were imaged in the acute phase (within 1 week of injury) as well as twice in the chronic phase (five or more months post injury). Eight patients had an additional acute session and eight were also imaged in the subacute phase of injury (more than 21 days post ictus). Eight controls underwent three imaging sessions over the same time period as the patients. Ethical approval was obtained from the ~~Local~~ Research Ethics Committee and informed assent/consent was obtained in all cases. MR imaging was performed using a 3 Tesla Siemens TIM Trio, and included a 3D T1-weighted structural sequence (MP-RAGE) with isotropic voxel size of 1x1x1mm. The T1-weighted images were preprocessed using the N4 algorithm to correct for intensity inhomogeneities[1]. The images were extracted with a brain mask calculated with pincram (pyramidal intracranial masking)[2]. A multi-atlas segmentation approach was used to segment MR images: The atlas cohort used in this study consisted of 30 manually annotated MR brain images of different subjects of the OASIS database[3] that had been manually segmented into 134 anatomical structures[9]. The brain atlases were aligned with the unsegmented brain scans to create subject specific segmentation estimates. MAPER was used for image registration[4], an approach which incorporates tissue probability maps into the registration and relies on a non-rigid registration based on free-from deformations (FFD)[5,6]. Using symmetric intra-subject registration[7] temporally corresponding scans were aligned. In an expectation-maximization (EM) framework (based on [8]) the availability of probabilistic segmentation estimates was exploited to perform a symmetric intensity normalization and segmentation. Symmetric differential bias correction for images in presence of pathologies was then performed. We achieved a consistent multi-time-point segmentation using a spatially and temporally varying Markov random field. Volumes for regions that are commonly damaged after TBI were extracted and compared to controls. Non-parametric statistics were used.

Results: The thalamus and cerebral white matter showed a significant volume loss over time for patients but not controls ($P<0.001$). The lateral ventricles showed a significant volume increase in the patient group ($P<0.001$). In contrast there was no significant volume change in the hippocampus for either patients or controls.

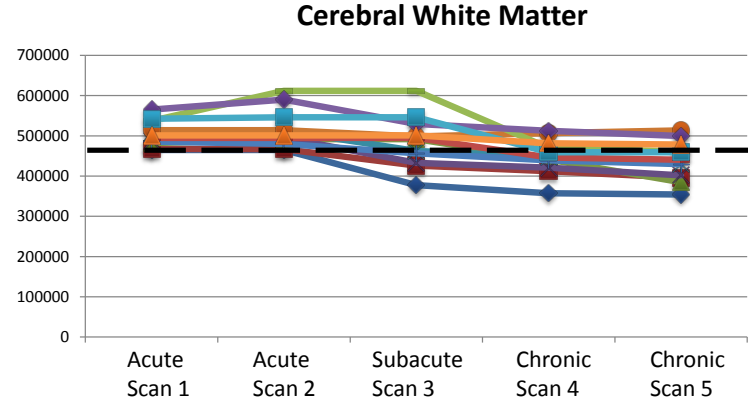

Figure 1: Example of changes over time in the cerebral white matter. The patients are represented by colored lines. The black dashed line shows the median for the control subjects. Early, when edema is present patients appear to show more white matter volume than controls. Over time, there is a decrease in white matter volume in patients. No similar decrease was seen in the control group.

Discussion: The differential effects of volume change are consistent with progressive but selective damaging effects of TBI on the white and grey matter, indicating that individual regions have different resilience and/or vulnerabilities to the effects of injury. The volume changes seen are likely secondary to the influence of edema in the acute scans. Late changes in regional volume are attributable to a range of pathophysiological process, including Wallerian degeneration, metabolic changes, and inflammation, all of which can contribute to progressive volume loss at late intervals. Such knowledge of longitudinal change is important to aid interpretation of imaging findings. These data can also provide further insight into the pathophysiology of TBI and may help to provide a framework that allows DTI to be used as an imaging biomarker of therapy response.

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