Parametric response map (PRM) is a promising tool for the monitoring of post traumatic cerebral edema

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Introduction

Cerebral edema (CE) is the key factor for the development of secondary brain injuries after severe traumatic brain injury (TBI). This edema may be assessed using the Apparent diffusion coefficient (ADC) measured by diffusion-weighted magnetic resonance imaging. One generally estimates ADC as the average value inside specific regions of interest (ROI), mainly grey matter. However, this approach does not take into account the complexity and the heterogeneity of the post traumatic edema. The parametric response map (PRM), a voxel-based analysis technique, is a promising tool to better investigate spatially dispersed changes of ADC over time [1]. In this study, we compare 2 methods of image analysis (ROI vs. PRM) to characterize the evolution of the ADC in the hours following a rat TBI.

Materials and Methods

Twenty three male Wistar rats were traumatized (400-500g) and eleven Sham operated rats were used for the control group. Anesthesia was induced and maintained with isoflurane (inhaled fraction of 2%). After tracheal intubation, rats were mechanically ventilated with 60% air–40% 0_2. Catheters were surgically inserted into the femoral vein and artery to permit the monitoring of blood gazes, blood pressure, and the administration of fluids. Maintenance of rectal temperature at 36.5±0.5°C was ensured, and End-Tidal CO_2 was continually monitored. Injury was induced using the impact-acceleration protocol as described by Marmarou in 1994 [2]. The reference time (H0) corresponded to the moment of the impact. MRI was performed at 7T in a horizontal bore magnet (Biospec 47/40 USR AV III, Bruker BioSpin, France). Diffusion-weighted images were acquired using an echo-planar, spin-echo, sequence. Parameters of the diffusion sensitization were: duration (δ)=1.39ms, separation (Δ)=15ms, b~0 (reference) or b=800s/mm^2. Seven adjacent rostrocaudal slices (1-mm thickness) were acquired (repetition time=2200ms; echo time=30ms; field of view=30 x 30mm^2; segments=2; acquisition matrix =128 x 128; 16 averages). Acquisition of one set of diffusion weighted images lasted about 8 min. Acquisitions were performed before the trauma, immediately after and every 30min. After 2h, rats were sacrificed. All images were co-registered to T2-weighted images acquired at H0 using a fully automated, normalized cross correlation algorithm (co-register function in SPM12 software). Following co-registration, a ROI was manually contoured including most of the brain, excepted edges and ventricles. For each rat, each time point and ROI, PRM was used to analyze, voxel-wise, changes in ADC. Briefly, PRM was performed by calculating the difference in the ADC values of each voxel in the ROI between the pre trauma acquisition (H-30) and the values of the other time points. A variation threshold (100 x10^{-6}mm²/s) was defined as the value below which 95% of the pixels in the Sham rats are considered as stable by the PRM analysis. Using this threshold, the fraction of voxels whose ADC significantly increased (PRM+: red), the fraction of voxels whose ADC significantly decreased (PRM-: blue), and the fraction of voxels whose ADC was unchanged (PRM0: green) were computed. We have red + blue +green = 100% of the voxel inside the ROI. In addition, the mean ADC inside the ROI was computed.

Results

The classical mean ADC value approach did not show any statistical differences between TBI group and Sham group (Fig.1). Yet PRM approach on the same groups detected edematous processes: TBI group presented statistically fewer green voxels than Sham group at every time point ($p<0.05$), with a dual increase of red and blue voxels (Fig.2). PRM analysis could also distinguish 2 sub-populations in the TBI group based on edema evolution: increase of mainly red voxels which is interpreted as vasogenic edema (Fig.3a) or mainly blue voxels which is interpreted as cellular edema (Fig.3b). Using PRM approach, we could also observe that TBI induces modifications of ADC that are not necessarily bilateral (Fig.3a, H2) and not restricted to the cortex and striatum that are the classical ROI for the mean ADC value approach.

Conclusion

PRM analysis is a valuable tool for analyzing the complexity of post traumatic CE and our data showed that a single model of experimental TBI induced several types of CE evolution. These findings could explain high standard deviations for mean ADC that is observed when the classical analysis is performed. PRM could permit to identify specific subgroups for future experimental trials.

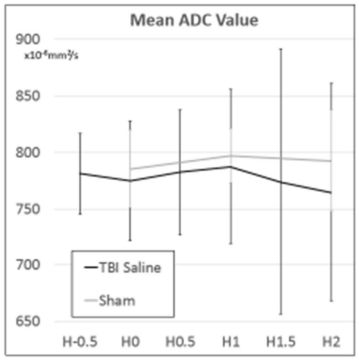

Fig.1

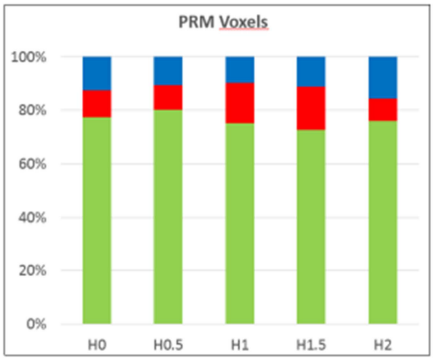

Fig.2

Fig.1 Evolution of mean ADC value within ROI over time in TBI (black) and Sham (grey) group. ($p>0.05$)

Fig.2 Qualitative representation of PRM voxels in TBI group, using the PRM approach.

Fig.3 Two different evolutions of cerebral edema: a) predominant vasogenic edema, b) predominant cellular edema.

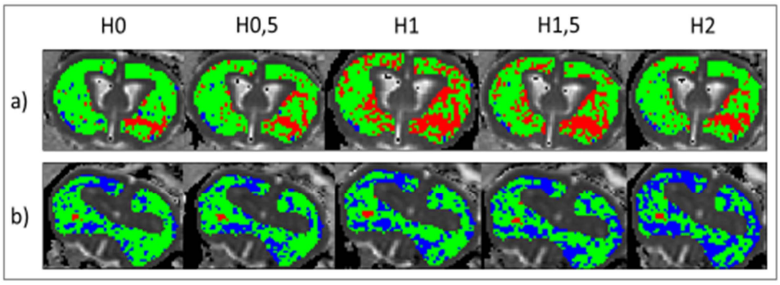

Fig.3

References

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2. Marmarou A, etal. J Neurosurg. 1994 Feb;80(2):291–300.