Cerebral blood volume alterations after traumatic brain injury in the rat brain - 2 weeks MRI follow-up

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Introduction

After the traumatic brain injury (TBI) the acute impact causes the primary injury, and the long lasting progression of damage is launched by the secondary injury cascades. One cause for the secondary injury may be the alterations in blood circulation, either compromised blood supply or increased blood flow, which in turn may strain the vulnerable vasculature. We studied the relative cerebral blood volume (CBV) changes in rat brain following cortical impact injury aiming to find out more about the hemodynamics in the perifocal area surrounding the lesion in acute (1-4 hours) and subacute (1-14 days) phase after TBI.

Methods

Traumatic brain injury was induced unilaterally to 62 male Sprague Dawley rats by controlled cortical pneumatic impact, while 12 rats served as controls. The MRI was performed 1 h (n=6), 2 h (n=12), 4 h (n=13), 1 d (n=6), 2 d (n=6), 3 d (n=6), 4 d (n=6), 7 d (n=6) and 14 d (n=14) after TBI. MRI data were acquired at 4.7 T using Varian Inova console and an actively decoupled volume transmission coil and quadrature surface receiver coil (Rapid Biomedical) before and after iron oxide contrast agent (Sinerem, 3 mg/kg) infusion into the femoral vein. T2* weighted images were measured using a gradient echo sequence (TE=15 ms, TR=1500 ms, flip = 70º, 128*256 pts), T2 weighted images using spin echo sequence (TE=70 ms, TR=2500 ms, 128*256 pts), and diffusion map, Dav=1/3 of the trace of the diffusion tensor, using a spin echo sequence (b-values=0,700,1000 $*10^{-3}$ mm^2/s, TE=60 ms, TR=2 s and 64*128 pts), FOV= 4.0*4.0 cm^2, 17 slices, slice thickness=1.0 mm and 2 averages per phase encoding step. The ΔR2 and ΔR2* maps were calculated from post-pre subtraction images and are here assumed to be directly proportional to CBV with a contribution of only small vessels (dia. 8-12 μm) or both large and small vessels, respectively. The statistical analysis is performed using Student's t-test, results are shown as mean±SEM.

Results

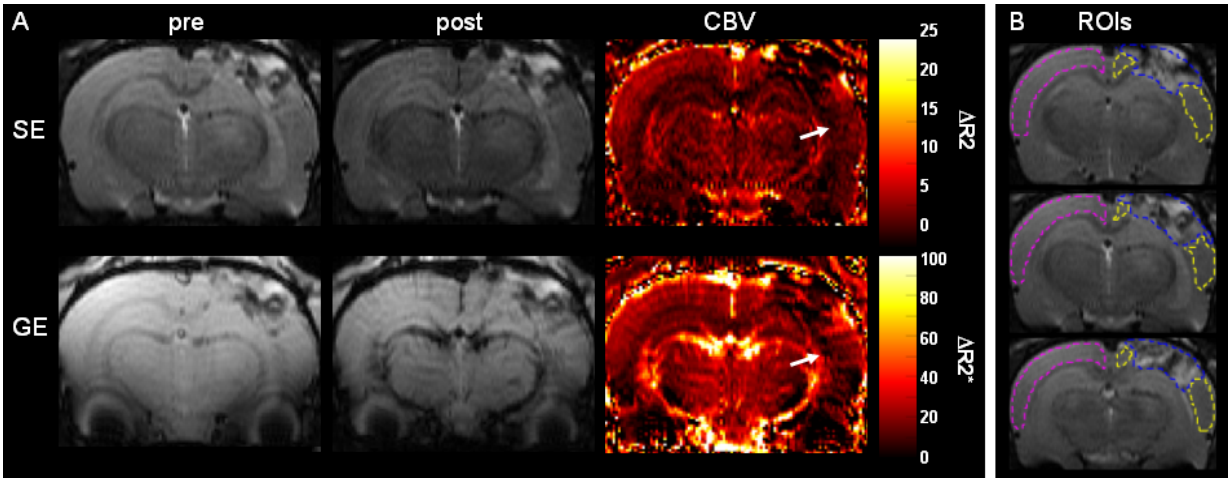

Fig 1. (A) Spin echo (SE, top row) and gradient echo (GE, bottom row) images pre and post contrast agent infusion and corresponding ΔR2 and ΔR2* maps from representative animal 2 d after TBI when CBV is decreased in perifocal area (arrows). **(B)** ROIs were outlined in T2 weighted images as follows: the whole lesion (blue, extending over 4-11 slices), perifocal area (yellow) and contralateral cortex (pink) in three consecutive slices around the lesion epicenter.

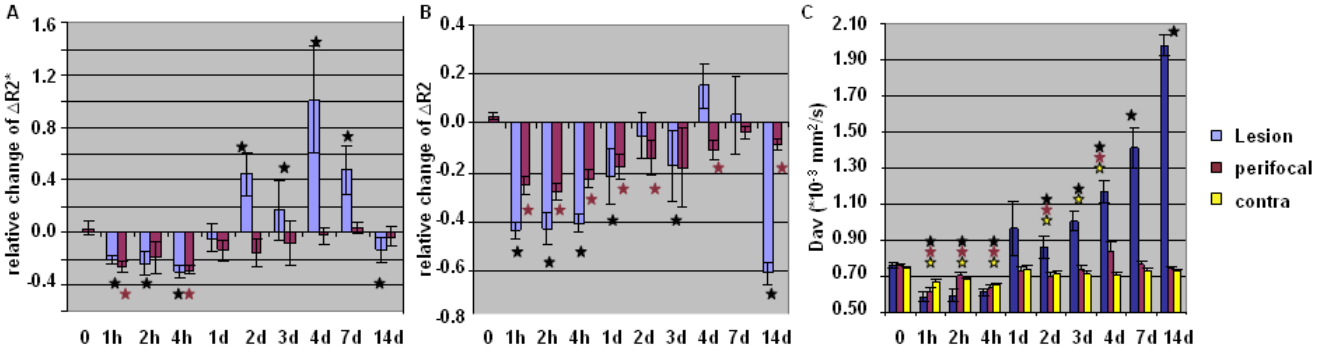

Fig.2. CBV and diffusion changes following TBI in lesion and perifocal area, values are normalized to the contralateral cortex. (A) Change in ΔR2 values represent the change in CBV in small vessels and (B) change in ΔR2* values represent the change in CBV in small and large vessels. (C) Diffusion (Dav) highlights the severity of tissue damage in lesion compared to the perifocal area (*, $p<0.05$ compared to the controls). In the perifocal area, characterized with moderate diffusion decrease in the acute phase and increase of 11% by day 4, the CBV drops acutely after TBI and slowly recovers thereafter. However, in the small vessels the CBV remains decreased even 14 d after TBI. In the primary lesion area, where the acute diffusion drop is followed by very evident increase of diffusion after day 4, CBV decreases acutely, shows increase in large vessels 2-7 d after TBI, and decreases again at 14 d.

Conclusions

Both ΔR2 and ΔR2* showed similar trends in the perifocal region, still the ΔR2 appeared to measure the CBV more consistently with smaller inter animal variation. When normalizing the data to the contralateral values, both ΔR2 and ΔR2* showed acute drop in CBV in the perifocal area, which then started to recover. Yet even after 14 d, ΔR2 remained decreased. In the primary lesion area, the interpretation of ΔR2 and especially ΔR2* data is complicated by the possible extravasation of the contrast agent. In the perifocal tissue CBV imaging with intravascular contrast agent is able to detect decreased CBV associated with hypoperfusion, which have a role in the secondary injury cascade, and may provide a potential target for developing novel drugs for treatment of traumatic brain injury.