Does decompression sickness lead to brain injuries?

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Introduction: When neurological damage occurs in divers the suspected primary cause is vascular gas bubbles. Entrapment of these bubbles may lead to cellular injury, cerebral oedema and increased permeability of the blood-brain barrier (BBB)[1,2]. Furthermore, studies of North Sea saturation divers have shown that divers report problems with concentration and memory more frequently than controls, and this can possibly be explained by CNS injuries[3, 4]. In this study, we have investigated effects of compression and decompression in a diving chamber on the rat brain using several MRI-protocols, including DTI, manganese-enhanced MRI (MEMRI) and dynamic enhanced MRI (DC-MRI), at several time points after decompression.

Materials and Methods: Rats (n=9) were compressed at a rate of 200kPa/min to a pressure of 700kPa, maintained for 45 min and then decompressed to the surface (100kPa) at a rate of 50kPa/min, breathing air throughout the procedure. Control rats (n=5) were kept at 100 kPa, breathing air for a similar time period. MRI was performed 1 hour, 7 days and 14 days after decompression on a 7T Bruker Biospec (Bruker Biospin, Germany) with a 72 mm volume coil for transmit and an actively decoupled rat head surface coil for receive. Rats were anesthetized with 1-2% isoflurane in 1:2 O_2/N_2. The MR-protocols were as follows: MRI acute: MGE T2*-map (TR=1650ms, TE=4-81ms, pixel size=156µm^2), RARE T2-map (TR=4000ms, TE=25-125ms, pixel size=156µm^2), EPI diffusion map (TR=3000ms, TE=53.5ms, pixel size=156µm^2, 6 b-values (100-1000s/mm^2) in 3 directions), RARE T1-map (TR=341-5000ms, TE=7.1ms, pixel size=156µm^2), RARE T1-weighted dynamic scan (TR/TE=350ms/7ms, 200 repetitions, pixel size=312µm^2, a bolus dose of 0.3mmol/kg Omniscan (GdDTPA) was injected through the tail vein after 10 baseline scans). 9-17 slices with 1 mm slice thickness were used for all scans. MRI 7 days: MGE T2*-map and RARE T2-map as above, EPI-DTI (TR/TE=3000ms/37.5ms, pixel size=156µm^2, b-values=0, 1000s/mm^2, 30 diffusion directions), MEMRI T1-w FLASH (TR/TE= 12ms/3.25ms, FA=30°, voxel size=156µm^3; 40mg/kg $MnCl_2$ injected i.p. 1 day after decompression). MRI 14 days: MGE T2*-map and RARE T2-map as above. DTI as above, but with slice thickness=0.5mm. Total scan time for each animal was 1-1.5 hours at each time point. Brain tissue was stained for HES, Map-2, Caspase 3, GFAP, MBP, Luxol fast blue and CD68. MRI data was analysed using FSL (Analysis Group, FMRIB, UK), SPM (Wellcome Dep. of Imaging Neuroscience, UK) and in-house build programs written in Matlab2009 (The Matworks, Inc). DCE-MRI was analysed by assuming a two-compartment model. Groups were compared using t-tests and found statistically different if $p<0.05$.

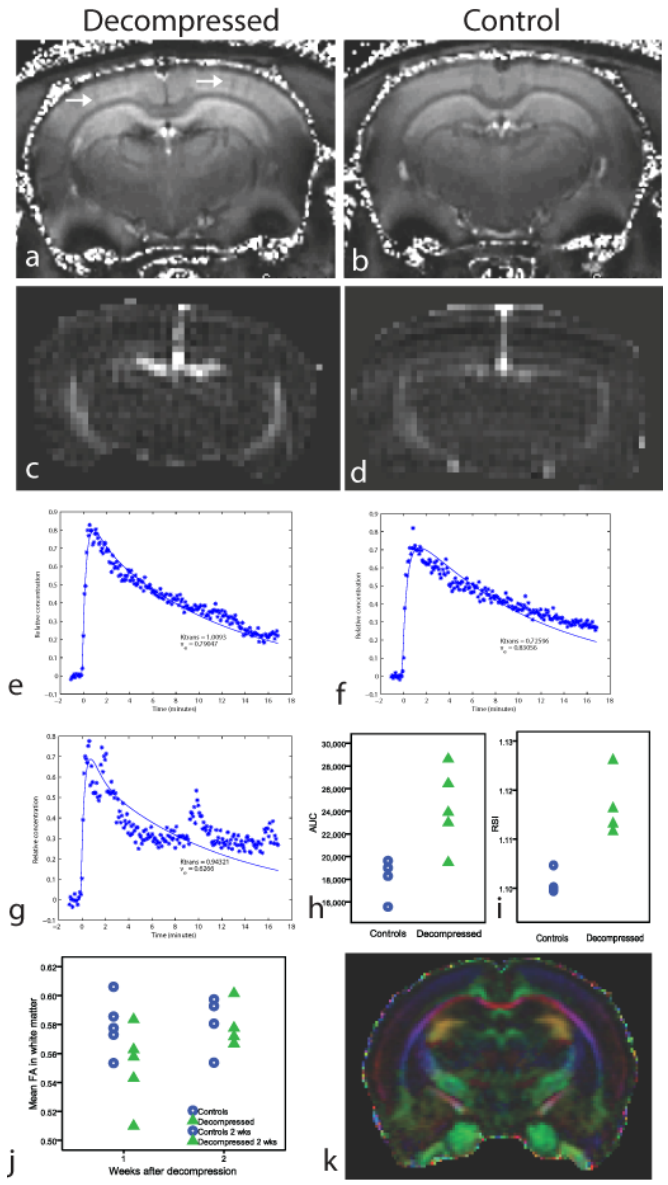

Figure 1: Some T2*-maps (a,b) had increased visibility of the veins (a, arrows). AUC-maps illustrating increased signal in decompressed rats compared to controls (c, d). Dynamic response (time vs relative concentration of contrast agent) in DCE-MRI was generally not different in decompressed rats (e) and controls (f). One decompressed rat displayed an abnormal dynamic response (g). AUC (h) and RSI (i) was increased in decompressed rats compared to controls. No differences were seen on mean fractional anisotropy after one or two weeks (j) and no injury was seen on DTI, here illustrated by a directionally color-coded FA-map of a decompressed rat brain (k).

Results: T2*-maps showed increased visibility of veins in some animals (fig. 1a, b), but no difference between groups. Voxel-based whole-brain analysis of DCE-MRI showed increased relative signal intensity (RSI) and area under the dce-curve (AUC) in decompressed rats compared to controls (p=0.002 and 0.015, fig. 1c, d, h, i). Dce-curves were in general similar in both groups (fig. 1e, f), but one of the decompressed rats displayed an abnormal dynamic response (fig. 1g). T2-maps showed no pathology and no differences between groups. Neither region-based nor voxel-wise analysis of MEMRI data showed any differences between groups. No injury was seen on DTI (fig. 1j, k), and parameters like fractional anisotropy, mean, axial and radial diffusivity were not different between groups. There were no apparent structural or cellular injuries, and no differences between the groups when analysing the immunohistochemically stained brain tissues.

Discussion and Conclusion: Extensive MR protocols at three time points after decompression of rats have been used to look for effects on the brain caused by decompression. Two rats died immediately after decompression, and one additional rat died after the first MRI (rat with abnormal dynamic response, fig. 1g), which indicates the severity of the decompression protocol. However, we did not detect any structural differences in the brain between decompressed rats and controls using MRI and histology. Dynamic contrast enhanced MRI demonstrated increased relative signal intensity and area under the dce-curve, meaning more enhanced voxels in the brain after decompression. This effect can be due to more contrast agent in the brain circulation, caused by for instance dilatation of brain vessels or increased perfusion. It can also be due to more contrast agent outside the vessels, indicating disruption of the blood-brain barrier.

In conclusion, severe decompression does not seem to cause any long term structural or cellular injury to the brain tissue, but may cause temporary changes in brain perfusion and integrity of the blood-brain barrier.

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