COMPARISON OF ISCHAEMIC LESION EVOLUTION USING DIFFUSION AND PERFUSION IMAGING IN THE SHRSP RAT AND WKY RAT FOLLOWING PERMANENT MIDDLE CEREBRAL ARTERY OCCLUSSION (MCAO).

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Introduction

The stroke prone spontaneously hypertensive rat (SHRSP) is a highly pertinent model of human ischaemic stroke. It has inherited cardiovascular risk factors, an increased incidence of spontaneous stroke, particularly on high salt diets and an increased sensitivity to experimental stroke compared to its normotensive reference strain (WKY) [1]. The mechanisms underlying this increased sensitivity to experimental stroke remain poorly understood. However, impairment in collateral flow to the ischaemic territory is thought to play a contributing role. To date nobody has investigated the evolution of permanent focal cerebral ischaemia in the SHRSP rat. In the present study we investigated the spatiotemporal evolution of ischaemic damage in the SHRSP rat and compared this to its normotensive control, the WKY rat. Diffusion and perfusion weighted MRI are extremely useful imaging modalities for the early detection of cerebral ischaemia and the diffusion/perfusion mismatch is the technique of choice for identifying penumbral tissue in stroke patients.

Methods

Male SHRSP (n=8) and WKY (n=8) rats aged 12-16 weeks of age were anesthetized with 1-2% isoflurane in a mixture of 70:30 N_2O:O_2, artificially ventilated and the middle cerebral artery permanently occluded (pMCAO) by the intraluminal filament technique. Imaging was performed on a Bruker Biospec 7T/30 cm system. A Spin-Echo based Echo Planar Imaging Diffusion weighted (DWI) scan (TE: 22.5 ms, TR: 4000.3 ms, 4 averages, matrix: 96 x 96, FOV: 25 x 25 mm, 3 directions: x, y, z, B values: 0, 55, 1055, 1055, 1459 s/mm^2, 8 contiguous slices of 1 mm thickness) revealed ischaemic damage. Perfusion weighted imaging (PWI) was carried out on a single slice through the MCA territory using a flow sensitive alternating inversion recovery (FAIR) sequence (TE: 50ms, TR: 12000ms, TI: 2000ms, flip angle: 90º, matrix: 96x96, FOV: 25 x 25 mm, slice thickness of 2mm). DWI and PWI were carried out every hour from 1 hour to 6 hours post MCAO. Apparent diffusion coefficient maps (ADC) and relative CBF (rCBF) maps were generated from the DWI and PWI images using Image J software and thresholded using previously published values [2,3] to allow assessment of the mismatch (Figure 1).

Figure 1. Representative ADC map, rCBF map and the mismatch between the ADC and rCBF abnormality following 1 hour pMCAO in the WKY. Injured tissue revealed on thresholded ADC map in red (tissue with ADC value below 80% of mean contralateral ADC). Perfusion deficit in red on rCBF map (threshold to ≥ 57% of the mean contralateral flow). Red shading on mismatch map reveals penumbral tissue 1hour after MCAO.

Results

The ADC derived lesion area increased in both the WKY and SHRSP over the entire 6 hour time course. The ADC derived lesion area was significantly larger in the SHRSP compared to the WKY from as early as 1 hour post MCAO (40.7 ± 6.2 mm^2 vs 30.1 ± 4.2 mm^2) and up until 6 hours post MCAO (Fig 2). In contrast, the perfusion deficit area was not significantly different between the two groups with the perfusion deficit remaining stable over the entire 6 hour timecourse. The diffusion-perfusion mismatch area was significantly smaller in the SHRSP compared to the WKY at all time points and was no longer present at 6 hours post-stroke (Fig 3).

Discussion

The present study demonstrates that SHRSP have significantly less penumbral tissue than WKY within 1 hour of stroke onset, in both strains penumbral tissue is recruited into the zone of ADC abnormality over time and by 6 hours, while WKY still display some remaining penumbral tissue, no perfusion/diffusion mismatch remains in SHRSP. These results could have important implications for the management of stroke patients with pre-existing hypertension and suggest ischaemic damage could progress at a faster rate in the presence of known risk factors such as hypertension. Further studies are planned to optimise the calculation of perfusion and diffusion thresholds and to investigate strategies designed to support penumbral tissue.

References

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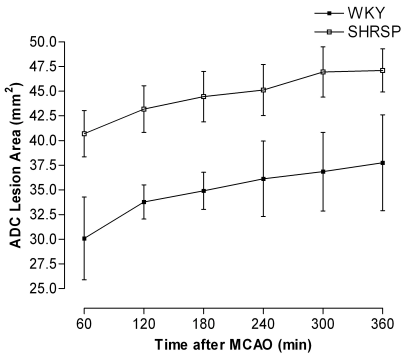

Fig 2. Temporal evolution of the apparent diffusion coefficient (ADC) derived lesion area (mm^2) in WKY and SHRSP rats following permanent MCAO. Data presented as mean±S.E.M (n=8 per group).

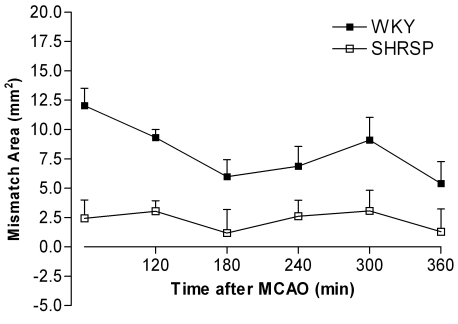

Figure 3. Temporal evolution of the mismatch area between the ADC and rCBF area in WKY and SHRSP rats following permanent MCAO. Data presented as mean+S.E.M (n=8 per group).