ADC correlates of CBF and Tissue PO2 in global cerebral ischemia

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Target Audience: Researchers in cerebral hypoxia, cerebral ischemia, ischemic thresholds and neuronal tissue viability

Purpose: Apparent diffusion coefficient is a highly sensitive marker for ischemic insult, but lacks desired specificity in distinguishing salvageable versus non-salvageable tissue. There is an ever urgent need to define ADC threshold correlates of cerebral blood flow (CBF) and tissue deoxygenation in ischemia. This study incorporated simultaneous tPO_2 measurement with interleaved perfusion and diffusion MRI at high temporal resolution to measure patterns of ADC changes in correlation to CBF and tPO_2 response immediately following global cerebral ischemia.

Methods: Five male SD rats (250-300 g) were studied. Fiber optic tissue pO_2 electrode (Oxford Optronix) was stereotaxically inserted into the left CPu (1.20 mm Bregma, 2.5 mm midline, 5 mm depth). Data was acquired during normoxia (5 mins 2% isoflurane in air), followed by global ischemia (35 mins, 5% isoflurane in N_2). CBF and ADC maps were acquired at 11.7 T using two-coil cASL (EPI-SE, TE/TR=14/2900 ms, 2-shot, labeling duration= 2.38 s, post labeling delay = 400 ms, scan time=12s) and DWI sequence (EPI-SE, TE/TR=23/3000 ms, b=0 and 1200 s/mm^2, scan time=12 s). 5 slices of FOV = 2.56x2.56 cm, 96x96 matrix, THK=2mm were acquired. The temporal resolution for the paired perfusion and diffusion acquisition was ~0.8 min (including dead time for scanner). Scans with prominent ghosting artifacts were excluded from time course. ADC, CBF and tPO_2 time courses were normalized from 0 to 1 for comparison. Data in text is group averaged mean ± SEM.

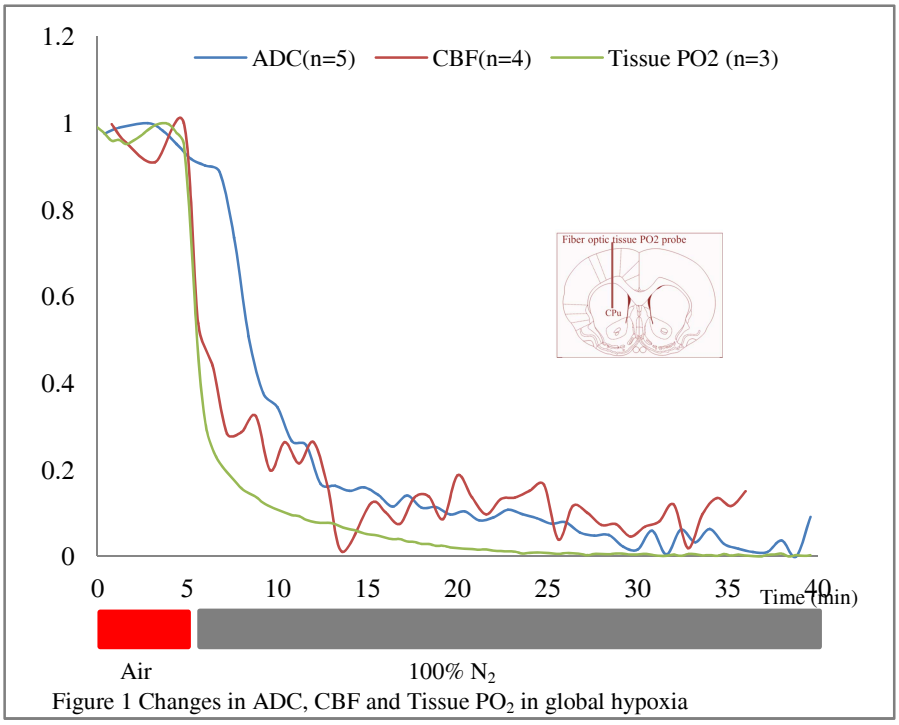

Figure 1 Changes in ADC, CBF and Tissue PO_2 in global hypoxia

Results: Under normoxia, the group-averaged ADC of the whole brain was 0.857±0.031 x10^{-3} mm^2/s (n=5), CBF was 0.67±0.094 ml/g/min (n=4) and tissue pO_2 was 35±10 mmHg (n=3). CBF and tPO_2 decreased immediately after onset of ischemia and closely followed each other (correlation coefficient: 0.98) in the initial phase. At CBF = 0.4 ml/g/min, the rate of change of CBF slowed down as compared to tPO_2. At CBF=0.2 ml/g/min, another change in decay rate of CBF was observed, after which rate of decay of CBF slowed down furthermore. By contrast, ADC did not show any change until CBF dropped below 0.4 ml/min/g. The rate of change of ADC was slower than CBF and tPO_2. We observed a second dip in the ADC at CBF threshold of 0.2 ml/g/min, after which the rate of decay of ADC slowed down furthermore **(Figure 1)**. Under global ischemia (35 min), mean ADC was 0.586±0.023 x10^{-3} mm^2/s, mean CBF was 0.171±0.063 ml/g/min and mean tissue PO_2 was 0.94±0.9 mmHg.

Discussion & Conclusion: Simultaneous measurement of ADC/CBF/tPO_2 with such high temporal resolution has led to some important findings. Changes in CBF and ADC are multiphasic whereas tPO_2 drops almost linearly in global ischemia. Initially the drop in CBF was well correlated with tissue deoxygenation. However, the rate of decay of CBF changed at 0.4 ml/g/min and 0.2 ml/g/min at which the rate of decay further slowed down. The ADC changes were less rapid as compared to CBF or tPO_2. ADC changed only after CBF fell below threshold of 0.4 ml/g/min. This initial change in ADC is likely attributed to dendritic swelling and swelling of perivascular astrocytic end-feet[1-2]. At CBF = 0.2 ml/g/min rate of change of ADC further slowed down, which is worth mentioning as this CBF threshold is also closely linked to disturbances in electrical activity of neurons at risk of infarction[3]. These multiphasic decay rates of ADC are likely attributed to changes in cellular diffusivity at distinct stages of ischemic cascade. High temporal resolution measurement of ADC and CBF was helpful to observe the multiphasic changes in ADC and CBF that otherwise remained unnoticed. Future studies will include reversible hypoxic injuries to determine ADC signatures of salvageable tissues in correlation to CBF, tPO_2 and local field potential.

References:[1] Miyasaka N, Radiology. 2000;215(1):199–204. [2] Haku T, Brain Research 2006;0:1–6. [3] Sharbrough F., Stroke. 1973;4:674-683