Correlation of Brain ADC Changes with Long-term Outcome after Cardiac Arrest.

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Introduction The quantitative mapping of apparent diffusion coefficient (ADC) is useful to characterize brain response to global ischemia. This imaging modality detects ischemia-induced changes that correlate with the intra- and extra-cellular water compartmentation, ionic equilibrium, and organized water movement. In this study, a rat asphyxial cardiac arrest (CA) and resuscitation model [1], fully compatible with MRI, was used to map the ADC changes continuously before, during and after cardiac arrest and resuscitation.

Methods The experimental protocol was approved by the Institutional Animal Care and Use Committee at the University of Pittsburgh and detailed elsewhere [1]. Ten anesthetized, paralyzed, male Sprague-Dawley rats, weighing 204–32 g, were placed in a specially designed cradle of a birdcage probe and positioned vertically (head up) inside the super-widebore, 9.4-T magnet of an Otsuka CMXW-400 spectrometer. The rat body temperature was controlled at 35 °C by air-heated blanket with feedback control. The cardiac arrest was induced within 29 ± 6 s of rapid iv injection of 8 mg/rat esmolol plus asphyxiation. Heating was discontinued during CA. In-magnet resuscitation after 16 min of asphyxia was achieved remotely by infusion of fresh donor arterial blood, mixed with epinephrine (8 µg/ml) and sodium bicarbonate (0.05 mEq/ml), into the femoral artery. Blood infusion was accomplished at a rate of 0.8 ml/min until the return of spontaneous circulation (ROSC) was observed. Diffusion-weighted images of the brain were acquired continuously before, during, and after the cardiac arrest and resuscitation. A modified single-shot 36 pulse multiphase Optimized Ultra-Fast Imaging Sequence (OUFIS) was used [2] (flip angle 12°, two rf refocusing, total number of echoes 72 per image, half-Fourier acquisition with zero phase at the 20th echo). Images were phase corrected and zero-filled once before FFT, yielding matrix of 128x128. Other acquisition parameters were: SW = 200 kHz, pw = 13.3 µs, TE = 30 ms, TR = 2 ± 1, NA = 20, and FOV = 4.5 cm. The quantitative cerebral ADC mapping was obtained by semi-logarithm fitting of 5 diffusion-weighted images acquired with varying b-factors, from 730 to 1300 s/mm². The temporal resolution for each ADC map was ~4 min. Five days after cardiac arrest rats were re-anesthetized and their brain fixed with 3% paraformaldehyde (pH = 7.4).

Results and Discussion All rats were resuscitated to ROSC within 3.3 ± 0.3 min. Mean duration of circulatory arrest was 18.9 ± 0.3 min. Five rats survived for >5 days after cardiac arrest, and five died within 24 h after resuscitation. Fig. 1 shows two representative sets of ADC maps, one taken from a rat survived for >5 days (Fig. 1A) and another from a rat died within 24 hours after CA (Fig. 1B). The gray scale is in unit of cm²/s. Before CA, the pixel-averaged ADC at this level of brain was 8.3±10⁻⁶ cm²/s. Immediately after cessation of circulation, ADC was reduced by 30% to 5.8±10⁻⁶ cm²/s, which is in an excellent agreement with the theoretical prediction that the perfusion accounts for about 30% of the ADC [3]. Continuing changes in ADC during CA after initial 30% drop, containing the pure diffusion component, may reflect ischemic changes in water/ions homeostasis and impairment of the intracellular water motion [4]. The five animals that died within 24 h after CA all showed scattered focal areas with severe decrease in ADC despite of global nature of ischemic insult (Fig. 1B). This could be explained by no-reflow phenomena in those areas. Fig. 2 shows the mean ADC, averaged separately among the survived and died animals, as a function of time. Survived animals showed complete recovery of ADC, whereas for rats that died within 24 h the decline in average ADC values correlated well with the shorter survival time. In the survived rats, only one showed typical ischemic changes in CA1 region of hippocampus (Fig. 3). The rats died within 24 h showed histological changes consistent with cerebral edema in the regions of decreased ADC. In conclusion, the quantitative ADC mapping provides precise measure of brain recovery after global ischemia. The development of the focal abnormalities in ADC maps in the first few hours after global brain ischemia correlates closely with the poor long-term survival in this particular model of global ischemia.

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Coronal sections (6 µm thick) at the level of dorsal hippocampus were prepared and stained with hematoxylin-eosin (H&E).

Fig. 1 ADC maps (level of dorsal hippocampus) before and during CA and after ROSC in rats that survived for >5 days (A) and those that died within 24 h (B).

Fig. 2 Pixel-averaged ADC before, during and after CA (Mean ± sem). * - significant difference between survived and non-survived groups at the same time point (P < 0.05).

Fig. 3 H-E stain of the CA1 region at the level where ADC maps were acquired. The neurons show typical ischemic changes, including cytoplasm hyper-eosinophilia and nuclear pyknotis(arrows).