

# Secondary or Gradual ADC Decline Following Reperfusion: Origins in Delayed Hypoperfusion

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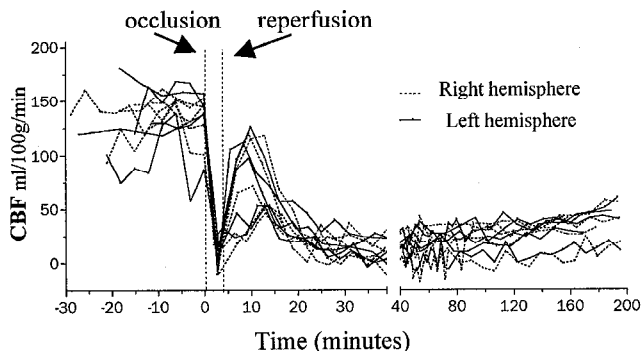
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**Introduction:** Following a brief period of ischemia/hypoxia, delayed tissue damage (1) or secondary energy failure (2) may occur. Animal studies of reperfusion have demonstrated that impaired cerebral blood flow (CBF) may develop following an insult. A few studies have suggested that a period of hypoperfusion is not pathogenic and therefore does not contribute to delayed damage (3). The aim of this study was to investigate the consequences of a brief period of global ischemia on CBF and the apparent diffusion coefficient (ADC) of water using perfusion- and diffusion-imaging

**Methods:** Bilateral common carotid occlusion was performed in 8 male Mongolian gerbils. Four minutes of global forebrain ischemia was produced via remote controlled occlusion of nylon snares placed around both carotid arteries, followed by approximately 4 hours of reperfusion. Experiments were performed on a horizontal 2.35 T magnet interfaced to a SMIS console. ADC measurements were obtained at 30 minute intervals using a single-shot trace-weighted EPI sequence [TE=110ms, TR=1000ms, avg=30, b-values = 0 and 1187s/mm<sup>2</sup>] (4). CBF images were collected using the FAIR technique with a spin-echo EPI sequence [TR/TI/TE=2800/1300/35ms]. A non-selective saturation pulse before each FAIR repetition enabled perfusion quantification without the need to wait for full relaxation. During the control phase of the experiment, a set of FAIR images were acquired at a range of inversion times and the data fitted to the standard bi-exponential in order to obtain the fixed parameters necessary for later flow quantification (5).

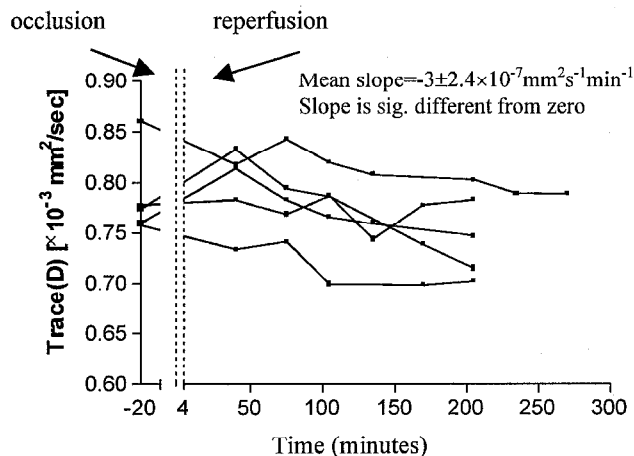
**Results:** On reperfusion two patterns of CBF and ADC changes were observed. Either a symmetrical bilateral pattern of flow impairment was observed (n=4) or an immediate side-to side difference became apparent with respect to the cerebral hemispheres (n=4). If the flow returned to normal following reperfusion then there were no subsequent ADC changes.

**Figure 1.** CBF time course before and after 4 minutes of ischemia



However, if delayed hypoperfusion developed (Fig.1) (CBF at 3h=35 ml/100g/min) subtle ADC changes were observed (Fig.2) (ADC change 5.7%), primarily in the striatum rather than cortex. This ADC decrease is only detectable when analysing the slope of the linear regression from the ADC data; ADC change is not detected with paired t-tests at individual time points.

**Figure 2.** ADC measurements before and after 4 minutes of ischemia.



**Discussion:** There have been several reports of ADC change following an ischemic insult, including a complete recovery of ADC on reperfusion (6), heterogeneous recovery of ADC on reperfusion (7), and a delayed decline in ADC (2). In our data, we observe a gradual ADC decrease, which is detectable using a regression analysis. Without the use of this analysis, ADC changes would not be apparent until later and may be classified as delayed changes, when in fact, subtle cellular changes have been taking place during the initial hypoperfusion phase. To our knowledge, this is the first demonstration of a gradual ADC decline during the hypoperfusion period, occurring subsequent to a brief period of ischemia. This may point to a period during hypoperfusion where intervention may be necessary in order to ameliorate recovery even though reperfusion has occurred.

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