The Sensitivity of Changes of Apparent Diffusion Coefficient of Cerebral Water to Outcome at 1 Year in Neonates with Suspected Hypoxic-Ischaemic Encephalopathy

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Synopsis: The sensitivity of ADC measurements in different regions of the brain to outcome at 1 year following suspected hypoxic-ischaemic encephalopathy (HIE) is examined. 15 term infants with suspected HIE were studied along with 6 healthy controls. Subjects were grouped according to their outcome at 1 year as assessed by neurodevelopmental testing. Regions of interest were defined within the deep grey matter and parietal, occipital and frontal white matter. White matter ADC is more sensitive to 1 year outcome than deep grey matter ADC at a median scan time of 4 days of age.

Introduction: Acute perinatal hypoxia-ischaemia is one of the primary potentially reversible causes of neonatal encephalopathy and subsequent cerebral palsy. The apparent diffusion coefficient (ADC) of water in the brain has been shown to reflect cerebral metabolic responses in the acute stages following ischaemic injury. However, there is currently some debate as to the ability of ADC to predict the extent of final injury[1]. Presented are results examining the sensitivity of regional measures of ADC within the brain to neurodevelopmental outcome at 1 year.

Methods: Studies were performed on a Bruker 2.4T Avance scanner using a diffusion-weighted segmented EPI sequence with automatic re-acquisition of motion corrupted segments[2]. This sequence was weighted to the trace of the diffusion tensor. An imaging slice was selected through the genu and splenium of the corpus callosum so as to intersect the basal ganglia. Two images (b=20 and b=600) were obtained and from these ADC maps were computed using a two-point log-linear fit.

Subjects and Analysis: Subjects were 15 term infants (mean corrected gestational age at scan (CGA) 40.3 ± 2.2 weeks; median postnatal age at scan (PA) 4 days [range 1-51]) with clinical signs of encephalopathy and a history consistent with perinatal hypoxia-ischaemia. Six healthy term infants (CGA 40.6 ± 1.2 weeks; median PA 2 days [range 1-6]) were studied as control subjects. All infants underwent neurological and developmental assessments at age one year and were divided into three outcome groups: normal, impaired with no disability (impaired) and impaired with disability (severe). Infants who had died by age 1 year subsequent to their neurological and developmental testing. Regions of interest were defined within the thalamus (T), basal ganglia (BG) and parietal, occipital and frontal white matter areas (PWM, OWM, FWM). The T and BG ADCs were combined to yield an average deep grey matter (DGM) ADC. ADCs from the white matter regions were combined to yield an average white matter (WM) ADC. Statistical testing was by ANOVA (single factor).

Results: The controls, who all had a normal outcome, were compared to subjects whose outcome was also normal. Significant differences were seen in T (p<0.01) and BG (p<0.05); no significant differences were seen in the WM. Comparison between outcome groups, excluding controls, showed significantly lower ADC in all regions in the severe group compared to the normal group (p<0.05). The graph shows average WM and DGM ADC. Using cut-offs of 2 standard deviations from the normal group-means, the DGM ADC identified infants with a severe outcome with a sensitivity of just 0.2; the WM ADC showed a sensitivity of 0.8.

Discussion: The DGM is known to be sensitive to global hypoxic-ischaemic insults[3] and the reduced DGM ADC in all subjects groups is a reflection of this. However, the DGM ADC was only mildly sensitive to neurodevelopmental outcome. It is also known that the drop in ADC subsequently re-normalises and so the median PA in this study (4 days) may be sub-optimal to observe differences between outcome groups in the DGM. The WM ADC was markedly more sensitive to outcome. There is some evidence in the literature that the evolution of ADC following global ischaemia is slower in WM than in DGM[4]; at age four days the WM ADC may be closer to its minimum yielding a greater sensitivity to 1 year outcome. These data suggest that the involvement of the WM in the pattern of injury confers an unfavourable prognosis. Thus regional quantitative ADC measurements could add complementary information to that available from other techniques, such as magnetic resonance spectroscopy, in the early neonatal period. However, their interpretation is difficult without a good understanding of the time-courses of ADC change in different parts of the brain following injury. There is therefore a need to obtain time-course information from neonates who present with hypoxic-ischaemic encephalopathy in order to understand how the timing of the scan relates to the prognostic value of the acquired data.