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Research Report

Infarct volume prediction using apparent diffusion coefficient maps during middle cerebral artery occlusion and soon after reperfusion in the rat

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ABSTRACT

Middle cerebral artery occlusion (MCAO) in rodents causes brain infarctions of variable sizes that depend on multiple factors, particularly in models of ischemia/reperfusion. This is a major problem for infarct volume comparisons between different experimental groups since unavoidable variability can induce biases in the results and imposes the use of large number of subjects. MRI can help to minimize these difficulties by ensuring that the severity of ischemia is comparable between groups. Furthermore, several studies showed that infarct volumes can be predicted with MRI data obtained soon after ischemia onset. However, such predictive studies require multiparametric MRI acquisitions that cannot be routinely performed, and data processing using complex algorithms that are often not available. The aim here was to provide a simplified method for infarct volume prediction using apparent diffusion coefficient (ADC) data in a model of transient MCAO in rats. ADC images were obtained before, during MCAO and after 60 min of reperfusion. Probability histograms were generated using ADC data obtained either during MCAO, after reperfusion, or both combined. The results were compared to real infarct volumes, i.e.T2 maps obtained at day 7. Assessment of the performance of the estimations showed better results combining ADC data obtained during occlusion and at reperfusion. Therefore, ADC data alone can provide sufficient information for a reasonable prediction of infarct volume if the MRI information is obtained both during the occlusion and soon after reperfusion. This approach can be used to check whether drug administration after MRI acquisition can change infarct volume prediction.

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1. Introduction

The rat intraluminal middle cerebral artery occlusion (MCAO)/reperfusion model is broadly used in preclinical studies of stroke (Macrae, 1992; McAuley, 1995). However, several factors account for a rather high degree of inter-animal variability in infarct volumes after transient intraluminal MCAO. The strain (Aspey et al., 2000; Oliff et al., 1995; Prieto et al., 2005; Walberer et al., 2006) and age of the animals (Sutherland et al., 1996), the surgical method (Huang et al., 1999; Zarow et al., 1997), surgical interventions causing infarction in territories of the internal (Kanemitsu et al., 2002) or external (Dittmar et al., 2003) carotid arteries, the extent of collateral circulation (Dittmar et al., 2003) and the efficacy of reperfusion contribute to infarct volume variability. This variability between animals can certainly be a source of bias when the effects of treatments are evaluated. Therefore, identification of the acute lesion and prediction of the subsequent fate of the ischemic tissue would help to compare treatment groups more accurately.

Multimodal magnetic resonance imaging (MRI) is nowadays widely available in experimental research and it is an excellent tool for imaging brain damage in ischemia. Various imaging techniques are used to obtain predictive information in experimental stroke (Farr and Wegener, 2010), among which perfusion- and diffusion-weighted MRI are the most useful techniques for detecting signs of acute brain ischemia. Prediction using critical thresholds over apparent diffusion coefficient (ADC) or cerebral blood flow (CBF) maps is used in human stroke (Arenillas, 2002; Thomalla et al., 2003). More complex algorithms have been developed to predict tissue fate in experimental animal studies that are based on a generalized linear model (Wu et al., 2007), the probability of infarct (Shen et al., 2005), improved iterative self-organizing data-analysis algorithm (Lu et al., 2005; Shen and Duong, 2008), and artificial neural network (Huang et al., 2010) or support vector machine (Huang et al., 2011). These methods provide a reasonably accurate prediction of the final infarct volume determined by T2 MRI or histology one or more days after MCAO. However, many of these algorithms are quite complex to implement and they use multimodal MRI information by combining perfusion and diffusion data, among other parameters. Nevertheless, ADC maps seem to provide valuable information for adequate prediction of the final tissue outcome, particularly in models with reperfusion (Bråtane et al., 2009; Huang et al., 2010; Leithner et al., 2011; Rosso et al., 2011), and they can be easily obtained. Previous predictive studies used permanent MCAO or transient MCAO, but for the latter they used information acquired after reperfusion while they did not use MRI during ischemia.

In the present study, we aimed to evaluate the value of acute ADC maps to predict infarct volume after MCAO/reperfusion in the Wistar rat. We measured ADC during MCAO and shortly after reperfusion since recovery of ADC has been reported after transient ischemia (Ringer et al., 2001).

2. Results

2.1. *ADC and T2 Maps*

For each subject, we constructed several maps with the ADC data obtained during MCAO and after reperfusion and with the final infarct volume determined from the T2 map at day 7. These maps are shown for individual rats (numbered 1 to 11) in Fig. 1. Group A (upper row) (rats 1 to 5) is the group used to compute the probability histograms and group B (bottom row) (rats 6 to 11) is the test group (see Section 5). During MCAO (Fig. 1A), all rats showed a decay of the ADCocc values in the right hemisphere and a corresponding increase in the relative ADC (rADC) values. In all cases the affected volume (see Table 1)

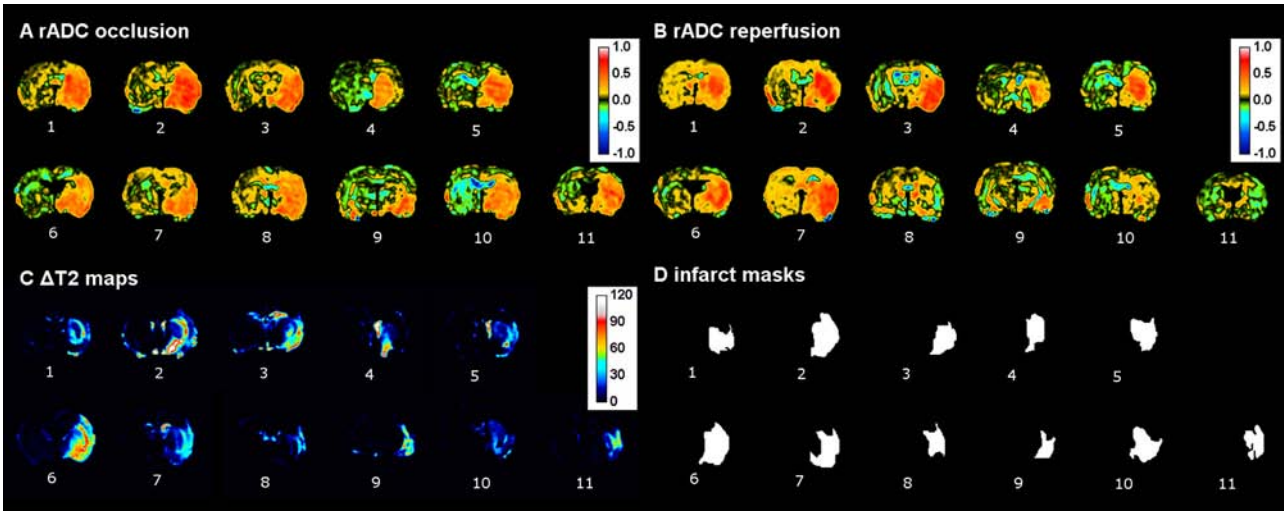

Fig. 1 – Coronal brain slices selected for each rat representation. (A) relative ADC maps at 60 min after occlusion, (B) relative ADC maps at 60 min after reperfusion, (C) difference in the T2 maps between the basal values before the infarct and the values 7 days after occlusion and (D) masks delimiting the final infarct from the T2 difference maps for two groups of rats. The first row shows group A with rats 1 to 5 used to compute the probability histograms. The second row shows group B with rats 6 to 11 as the test group. The number below each brain image is that of the rat.