The effect of cocaine on the rat brain apparent diffusion coefficient, cerebral blood volume and mean arterial blood pressure.

C. Du[1], Y. Ma[1], B. Forester[1], M. Yu[1], H. Benveniste[1,2]

[1]Medical, Brookhaven National Laboratory, Upton, NY, United States, [2]Anesthesiology, Stony Brook University, Stony Brook, New York, United States

Background: It has been reported in humans that acute as well as chronic cocaine intake can reduce cerebral blood flow as well as perfusion to other body organs (1-2). The mechanisms underlying these changes are still not fully understood. *In vitro* studies (3) in canine cerebral vascular smooth muscle cells have revealed that cocaine causes the cells to shrink to two-thirds of their original sizes. Other animal studies obtained by ^{31}P NMR and angiography have further shown that cocaine can induce vaso-constriction in both cerebral and peripheral vessels. We hypothesized that if cocaine induces vasoconstriction and reduces cerebral perfusion then the apparent diffusion coefficient (ADC) might also decrease if low (ischemic) perfusion thresholds were reached. The present study examined the effects of an acute cocaine challenge on changes in the rat brain ADC in parallel with measurements of cerebral blood volume (CBV) changes using a newly developed optical system.

Methods: Anesthetized Sprague-Dawley rats were used. The femoral artery was cannulated for continuous blood pressure monitoring and the femoral vein for administration of cocaine. In Group 1 rats a small craniotomy was made above the somatosensory cortex and an optical fiber probe was placed in contact with the cortical surface to measure the cocaine-induced changes in CBV. In Group 2 rats diffusion-weighted MR images were acquired every 4-min on a 9.4T 9.4T/20-cm horizontal magnet interfaced to an AVANCE console (Bruker) to assess potential early ADC changes associated with an acute cocaine challenge (1mg/kg). All hemodynamic parameters were continuously measured before, during and 30-min after the intravenous cocaine injection.

Results:

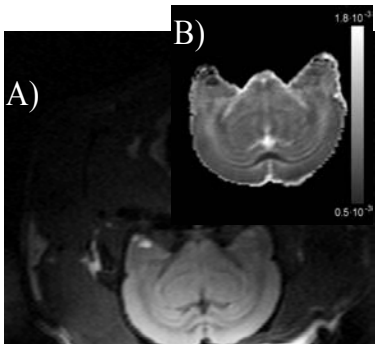

Fig. 1. A. Diffusion weighted MRI (A) and corresponding ADC map (B); in-plane resolution: 0.3 X 0.3 mm; slice thickness 1.8mm; TR/TE=400ms/20ms; b-values:125, 250, 400 and 1000 s/mm^2;scan-time: 3min 24s.

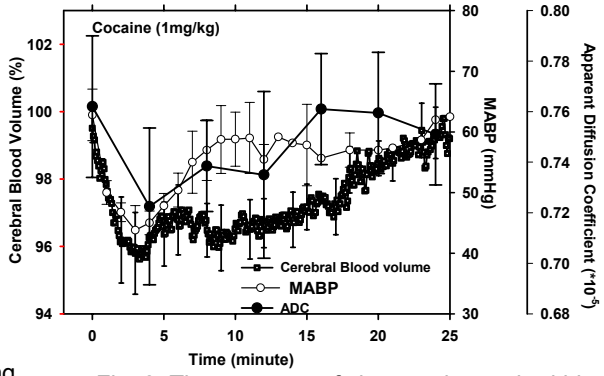

Fig. 2. Time courses of changes in cerebral blood volume, mean arterial blood pressure and cortical ADCs in response to an acute cocaine injection.

Fig. 2 shows that cocaine induces a rapid, small transient decrease in the cortical ADC (from 0.77±0.07 x 10^{-5} mm^2/s to 0.72±0.03 x 10^{-5} mm^2/s) in parallel with decreases in the cerebral blood volume and the MABP. Fig. 2 further shows that the MABP recovers back to normal within 5-6 min whereas the cerebral blood volume is decreased for >15 min suggesting that the early ADC decrease is a consequence of the MABP decrease. The ADC measurements in cortex does not reach ischemic (<0.4x10^{-5} mm^2/s) thresholds. The significance of our findings will be discussed in relation to the temporal resolution and volume averaging effects of our MR measurements in comparison with high temporal resolution optical data.

1. Brown E, Prager J., Lee H-Y, Ramsey RG. AJR 1992:159:137-147;
2. Holman BL, Carvalho PA, J Nucl Med 1991, 32: 1206-1210.
3. He GQ, Zhang A, Altura BT, Altura BM, J Pharmacol Exp Ther 1994, 268(3):1532-9.

Acknowledgement: Office of Science, Department of Energy