Cerebral Perfusion in Craniosynostotic Rabbits using ASL_MRI

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INTRODUCTION

Craniosynostosis is the premature fusion of one or more of the calvarial sutures and is estimated to occur in 300-500 per 1,000,000 live births [1]. Premature closure of the cranial suture has two main consequences: aesthetic deformity and the possibility of secondary damage of the growing brain. Neurologic injuries associated with craniosynostosis can result from increased intracranial pressure (ICP) [2,3] and abnormal cerebral blood flow (CBF) [4]. A clearly defined view of the relationship between the brain and skull vault growth is lacking. It becomes clear that the mechanisms behind craniosynostosis are not clearly understood and that the study of the natural progression of uncorrected craniosynostosis could provide valuable information regarding the brain and its ability to compensate for skull restriction when present. The present study was undertaken to study age-related CBF differences in a homogenous strain of rabbits with early onset coronal-suture synostosis (EOCS) and compare with age-matched wild-type (WT) controls.

MATERIALS AND METHODS

The rabbits used were bred in the vivarium at the Department of Anthropology, University of Pittsburgh. Rabbits were divided into the following experimental groups: WT control rabbits at 10 days of age (n=6); EOCS rabbits at 10 days of age (n=6); WT rabbits at 25 days of age (n=6); EOCS rabbits at 25 days of age (n=5); WT rabbits at 42 days of age (n=4); and EOCS rabbits at 42 days of age (n=4). Physiological parameters such as heart rate, and arterial CO_2 tension ($PaCO_2$), and body temperature were monitored throughout the study. The rabbits were placed on the cradle in a prone position and the head secured by ear bars and a bite bar to prevent motion during imaging.

MR studies were performed on a 4.7-Tesla, 40 cm bore Bruker AVANCE-AV system, equipped with a 12 cm diameter shielded gradient insert and a 72 mm volume RF coil. For all imaging experiments, an FOV = 6.4 cm and slice thickness = 2 mm were used. Maps of T_{1obs} [5] were generated from a three-parameter exponential fit to a series of spin-echo images with variable *TR* (*TR* = 8000, 4300, 2300, 1200, 650, 350, 185, 100 msec, 2 averages, 128 x 70 matrix). Perfusion spin-echo images were acquired in duplicate using the arterial spin-labeling technique [6] (*TR*/*TE* = 2000/10, 20, 30, summation of 3 echoes, 2 averages, 128 x 70 matrix) with labeling applied ± 2.5 cm from the imaging plane. CBF (cerebral blood flow) maps were generated from: $CBF = \lambda \cdot (T_{1obs} \cdot 2\alpha)^{-1} \cdot (M_C - M_L) \cdot (M_C)^{-1}$, where M_C and M_L are the magnetization intensities from the control and labeled images, respectively. A spatially constant value of 0.9 mL $\cdot$ g^{-1} was assumed for the blood brain partition coefficient for water (λ). The spin labeling efficieny (α) [7] was determined in each study with gradient echo images with spin-labeling applied at ± 11 mm (*TR*/*TE* = 100/9.6 msec, 45° flip angle, 8 averages, 256 x 256 matrix).

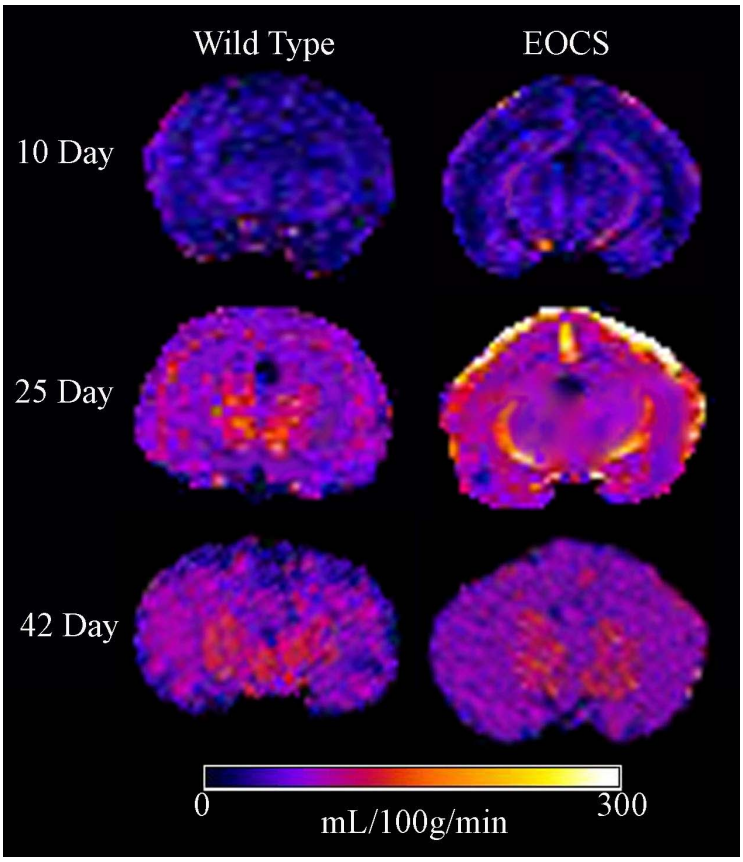

Figure 1. Representative CBF maps from wild-type and EOCS rabbits at or near 10, 25, and 42 days of age.

RESULTS AND DISCUSSION

Our results demonstrate that CBF was not different in rabbits with EOCS when compared to age-matched wild-type rabbits. The increase in both groups seen between 10 and 25 days of age is the normal pattern of CBF in the immature brain [8].

Remarkably EOCS rabbits at 25 days of age displayed areas of high CBF on the peridural surfaces of the brain. This coincides with the time of increased intracranial pressure previously reported in this colony of rabbits [2]. During intracranial hypertension the pial arteries not only remain open, but even dilate because of smooth muscle relaxation [9]. The results of the present study agree with this finding. By 42 days of age however, CBF in EOCS rabbits had decreased to normal adult range and the pial vasculature no longer demonstrated high CBF. We know from previous studies that ICP also returns to normal in EOCS rabbits between 25 and 42 days of age [2].

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REFERENCES

1. Cohen, M. M. Jr and MacLean, R. E. *Craniosynostosis: diagnosis, evaluation, and management.* New York: Oxford University Press, (2000).
2. Fellows-Mayle, W. K., Mooney, M. P., Losken, H. W. , Dechant, J., Cooper, G. M., Burrows, A. M., Smith, T. D., Pollack, I. F. and Siegel, M. I. *Cleft Palate Craniofacial J* **37**, 370-378, (2000).
3. Fellows-Mayle, W., Hitchens, T. K., Simplaceanu, E., Horner, J., Barbano, T., Nakaya, K., Losee, J. E., Losken, H. W., Siegel, M. I. and Mooney, M. P. *Childs Nerv. Syst.* **21**, 385-391, (2004).
4. Sen, A., Dougal, P., Padhy, A. K., Bhaltachaya, A., Kumar, R., Bal, C., Saspai, M., Bharadwaj, M., Mitra, D. K., and Basu, A. K. *J. Nuclear Med.* **36**, 394-398 (1995).
5. Hendrich KS, Kochanek PM, Williams DS, Schiding JK, Marion DW and Ho C. *Magn. Reson, Med.* **42**, 673-681 (1999).
6. Detre JA, Leigh JS, Williams DS and Koretsky AP. *Magn. Reson. Med.* **23**, 37-45 (1992).
7. Zhang W, Williams DS and Koretsky AP. *Magn, Reson, Med.* **29**, 416-421 (1993).
8. Tuor, U. I. *Ped. Res.* **29**, 517-523 (1991).
9. Auer, L. M., Ishiyama, N., Pucher, R. *Acta Neurochir* **84**,124-128 (1987).