

## CORRESPONDENCE

*To the Editor:* In the December issue of Pediatric Research, Jayasinghe et al. (1) tested the hypothesis that CBF reactivity to changes in MAP (cerebral autoregulation) or CO<sub>2</sub> (CO<sub>2</sub> reactivity) is lost in hypotensive, ventilated, preterm infants. The investigators report a difference in MAP-CBF reactivity and CO<sub>2</sub>-CBF reactivity among normotensive and hypotensive infants. Specifically, the authors report higher MAP-CBF reactivity, reflecting impaired cerebral autoregulation, and attenuated CO<sub>2</sub> reactivity in hypotensive infants compared to normotensive infants.

There are some methodologic issues with this study that merit discussion. First, there is no information regarding how CO<sub>2</sub> reactivity was formally examined, leaving the reader to assume that aggregate and random CO<sub>2</sub> - CBF data were analyzed. Second, although 95% confidence intervals were used to detect differences between groups, a Type II error cannot be ruled out in the normotensive MAP-CBF group, particularly when the average reactivity was numerically equal in both groups. Third, no definitions for what constitutes impaired versus intact cerebral autoregulation was provided, making it difficult to interpret the differences between the normotensive and hypotensive groups. Fourth, although statistical analyses were used to normalize skewed data, it is not clear why a larger number of subjects was not used in each group. Given the small sample size of the study, it is not surprising that the variances were large. Finally, it is to be expected that cerebral autoregulation was impaired or abolished in hypotensive subjects since by definition, MAP in the hypotensive group is likely to be below the lower limit of cerebral autoregulation (LLA). Therefore, it is not clear why the authors would study something that is to be expected. Finally, although the authors state that the LLA in preterm infants is 30 mmHg (2), the subjects of the present study were older (>23 months). The one paper describing the LLA in infants outside the neonatal period reports LLA values comparable to that of older children (3).

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1. Jayasinghe D, Gill AB, Levene MI 2003 CBF reactivity in hypotensive and normotensive preterm infants. *Pediatr Res* 54:848-853
2. Tyszczyk L, Meek J, Elwell C, Wyatt JS 1998 Cerebral Blood Flow is Independent of Mean Arterial Pressure in Preterm Infants Undergoing Intensive Care. *Pediatrics* 102:337-341
3. Vavilala MS, Lee LA, Lam AM 2003 The lower limit of cerebral autoregulation in children during sevoflurane anesthesia. *J Neurosurg Anesthesiol* 15:307-312

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*To The Editor:* We would like to thank Dr. Vavilala and colleague for their interest in our manuscript. Their letter raises a number of points primarily concerning the methodology of our study (1).

The first question they raise is how CO<sub>2</sub> reactivity was examined. The multiple-regression model used paired values of blood pressure and PaCO<sub>2</sub> measured contemporaneously with CBF measurements (1). In this way, we hoped to determine the individual effects of these predictor variables on our outcome variable (CBF).

The question of Type II error would be relevant if statistical comparisons were made between CBF reactivity of the two groups (which we do not do). In the main, we only compared biographical and physiological data between the two groups (Table 2 and 3), and it is in these cases only that one could not exclude Type II errors.

In the final paragraph of the Methods we define CBF-reactivity and in the Discussion we speculate with others as to whether autoregulation remains intact. As stated in our paper (1), this is based on whether the confidence limits encompass zero in the case of MAP-CBF reactivity, implying no change in CBF (2).

Dr. Vavilala is correct in that our study was of a small sample size. This reflects the difficulties of conducting clinical research in a population of the sickest preterm infants; inevitably, this leads to larger confidence limits.

Perhaps the most pertinent question raised by Dr. Vavilala is that of the lower limit of autoregulation in preterm infants. There exists a multiplicity of normograms used to define the normal range of blood pressure of preterm infants. It follows that there is no universally agreed definition of hypotension, and hence no definition of the lower limits of autoregulation. In essence, our paper tested one definition (3) and found impaired CBF reactivity in infants considered to be hypotensive by this definition. Other authors have tested other definitions (4).

The final point made by Dr. Vavilala is well taken as the first sentence of the results is somewhat misleading, and should have stated that the study was conducted over a 23-month *period*. However, throughout the rest of the paper it is made

quite clear that we studied a population of preterm infants during the first week of life (Table 2).

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