Resting State fMRI revealed differences in connectivity to visual cortex in premature infants with hypercapnic ventilation

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Introduction

Permissive hypercapnia is a common ventilation strategy widely applied to the neonatal intensive care of premature infants born with extremely low birth-weight (ELBW). This method, by permitting relatively high arterial partial pressure of carbon dioxide (PaCO2), is believed to prevent ventilator-induced lung injury in ELBW infants. However, PaCO2 is a potent regulator of cerebral blood flow (CBF), and hypercapnia in premature infants has been associated with impaired cerebral autoregulation and increased risk of intraventricular hemorrhage (IVH) (1). Therefore, the effects of permissive hypercapnia on the fragile and developing brain in ELBW infants need more investigation.

Resting state functional MRI measures the spontaneous low frequency blood-oxygen-level-dependent (BOLD) fluctuation in the brain and reveals the functional connectivity in brain network by correlation studies. Functional connectivity has been found in visual, auditory, and sensorimotor areas in the brain of sleeping infants (2). Resting state connectivity study by fMRI has also been shown feasible in extremely low gestational age infants at term-equivalent.

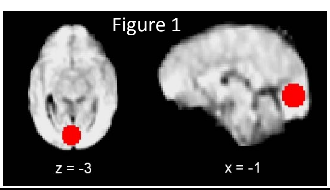
Hypercapnia has been observed to reversibly suppress the low frequency fluctuation in the motor cortex (3); similar results were reported by near infrared spectroscopy that spontaneous low frequency oscillations of cerebral hemodynamics in the visual cortex of adults were attenuated by hypercapnia (4). These findings suggest that permissive hypercapnia may affect the functional connectivity in the brain in ELBW infants. Therefore, we performed resting state fMRI study on ELBW infants randomized to groups with or without permissive hypercapnia and compared the functional connectivity in the brain to the primary visual cortex.

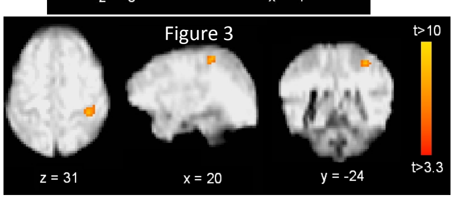
Methods

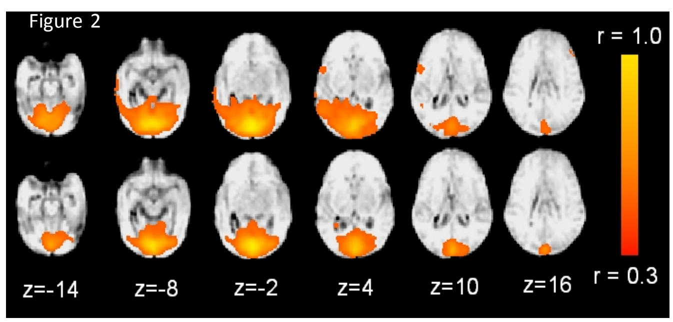
ELBW infants with birth weight 401-1000 g (gestational age < 30 weeks) were recruited and randomized to hypercapnic ventilation (50-60 mm Hg, N = 5) and normocapnic ventilation (35-45 mm Hg, N = 4) during the first week of life. All infants had MRI examination which included a successful 3D T1-weighted and a resting state fMRI study. MRI was performed at term-equivalent age on a 1.5 Tesla Philips Achieva scanner with an 8-channel SENSE coil. No sedation was used. The infants were fed ~30 minutes before the MRI and were scanned during natural sleep. The resting state fMRI data was acquired using a single-shot gradient echo EPI sequence with T2*-weighting, repetition time of 2 seconds, 2 dummy scans, 150 dynamics, and an imaging resolution of 2 mm x 2 mm x 4 mm. The 3D T1 and gradient echo EPI images were exported to a workstation with Analysis of Functional NeuroImages (AFNI) software (NIMH, Bethesda, MD, USA) for the resting state functional connectivity analysis. A standardized anatomic template was constructed from the 3D T1 images from the ELBW infants using DARTEL. The functional connectivity analysis involved selection of a primary visual seed region, and mean signal time courses of each seed region were used to perform correlation analysis throughout the brain to identify functionally connected regions with high temporal correlation. A connectivity map based on the strength of correlation was generated for each subject and co-registered to and displayed on the anatomical template. The average connectivity map for each group was also generated and the differences in connectivity to the primary visual cortex between the two groups were calculated by t-test.

Results

Figure 1 shows the seed region in the primary visual cortex for the connectivity analysis. The average visual connectivity maps for the hypercapnic (top) and normocapnic (bottom) groups are illustrated in figure 2, with a threshold for correlation >0.3. Neurological convention instead of radiological convention is used for the left and right. The difference between the two groups is illustrated in figure 3, with p<0.005 before multiple comparison correction and a cluster size threshold of at least 32 voxels. It was found that normocapnic infants had greater functional connectivity between the visual cortex and the right primary motor cortex (mean r=0.08) than hypercapnic infants (mean r=-0.06; two-tailed t(7)=4.4, p=0.0033).







Conclusion

We report decreased inter-network functional connectivity between visual cortex and motor cortex for hypercapnic infants compared to normocapnic infants. These findings suggest that hypercapnic ventilation may reduce functional connectivity between brain default networks. Future study with larger sample size is warranted to confirm these findings and to investigate resting state connectivity to other important functional networks in these two groups of ELBW infants.

References

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