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ASSESSMENT OF THE NUMBER OF NEURONAL PROGENITOR CELLS IN THE BRAIN OF FORMER PRETERM LAMBS

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Purpose of study: Although brain injury happens in chronically ventilated preterm infants, pathogenic mechanisms remain to be identified in part because brain tissue is not typically part of clinical material for study. We showed that preterm lambs supported by mechanical ventilation (MV) have more apoptosis, and less proliferation, of neurons and glial subtypes compared to non-invasive support (NIS). These results suggest that cell survival may be decreased in the brain of preterm lambs that are managed by MV. Disruption might lead to shift to more progenitor cells as a compensatory response. Neural stem cells give rise to neuronal progenitor cells, which are identifiable by doublecortin. We hypothesized that decreased neuron survival during MV may increase the number of neuronal progenitor cells in the brain.

Methods used: Preterm lambs, treated with antenatal steroids and postnatal surfactant, were managed by MV or non-invasive support for either 3d or 21d (n=4/group). We use non-invasive support (NIS, by high-frequency nasal support) as the positive gold-standard for alveolar formation in the lung. At the end of 3d or 21d of respiratory support, cortical brain tissue from the temporal lobe was fixed. We used immunohistochemistry to localize doublecortin-positive neuronal progenitor cells. We used stereology to quantify numerical density of doublecortin-positive neurons in Layer II, using systematic, uniform, random sampling.

Summary of results: We found no difference in numerical density of doublecortin-positive neuronal progenitor cells in cortical Layer II of the temporal lobe at 3d (PT MV $2.4\pm0.3\times10^5$ µm and PT NIS $2.9\pm0.5\times10^5$ µm, respectively) or 21d (PT MV $2.1\pm0.2\ 10^5$ µm and PT NIS $2.7\pm0.5\times10^5$ µm, respectively) between the two modes of respiratory support.

Conclusions: We conclude that MV of preterm lambs for 3d or 21d does not alter the number of neuronal progenitor cells in layer II of the temporal lobe of the brain. Current analyses are quantifying doublecortin-positive neuronal progenitor cells in white matter and in the periventricular zone.