The FASEB Journal

Fetal Brain Development Involves Activation of Inflammatory Pathways in the Fetal Cerebral Cortex: Increased Tissue Content of Interleukin 1β

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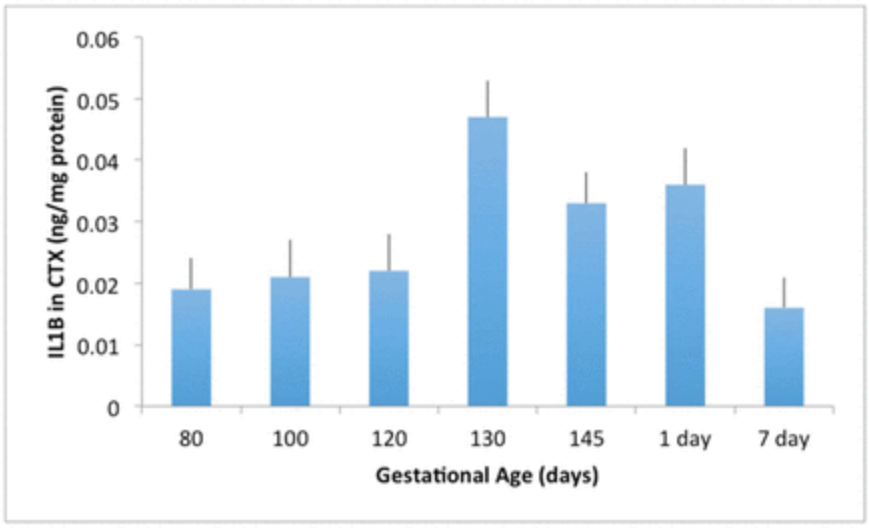
Published Online: 1 Apr 2016 **Abstract Number:** 1247.17

Abstract

Using transcriptomics methodology and systems biology modeling, we have previously reported that, in several regions of the fetal brain (cerebral cortex, hippocampus, hypothalamus, and brainstem), there is an increase in the expression of genes involved in immune function (especially within the hematopoietic lineage). We have also previously reported that there is an endogenous increase in expression of prostaglandin biosynthetic genes and proteins in hypothalamus and hippocampus, and that there is an increase in tissue concentrations of prostaglandin E2 (PGE2) in late gestation. We performed the present study to test the hypothesis that there are complementary signs of increasing brain inflammation in late gestation as a normal consequence of in utero development and readiness for birth. In the present study, we test the hypothesis that in the fetal cerebral cortex there is an increase in Interleukin-1β protein concentration at the end of gestation. Time-dated pregnant ewes (n=3–5 at each age) were sacrificed at 80, 100, 120, 130, and 145 days gestation (term=147 days), and we sacrificed lambs on day 1 and 7 of neonatal life. Tissue samples were taken at necropsy and flash frozen in liquid nitrogen for protein and mRNA analysis. Samples of cerebral cortex were homogenized in a reducing buffer for protein analysis. IL 1β protein was measured by ELISA in these samples using the Ovine Interleukin 1β kit from Genorise Scientific. Protein concentration in homogenates were measured using the Bradford technique. IL1β concentrations were normalized to protein concentrations. We found that tissue concentration of IL1β increased from 19±5 pg/mg protein at 80 days to a peak of 50±6 pg/mg protein at 130 days, then remained high through the first day of neonatal life (36±6 pg/mg protein), and returned to lower levels by 7 days of neonatal life (16±5 pg/mg protein). These changes were statistically significant as tested by ANOVA ($p<0.05$). We conclude that, concomitant with increases in immune development and increased expression within prostaglandin biosynthetic pathways, there is an increase in IL1β peptide in the late-gestation fetal brain. We speculate that increases in both the prostaglandin and interleukin systems are downstream of activation of inflammatory pathways within the developing fetal brain.

Support or Funding Information

This work was supported by NIH grants R01 HD033053, R01 HD057561, and R25 HL103181.



Ontogeny of IL1β protein concentrations in ovine fetal cerebral cortex throughout the latter half of gestation and early postnatal life.

Footnotes

- This abstract is from the Experimental Biology 2016 Meeting. There is no full text article associated with this abstract published in The FASEB Journal.