# Impact of Postanatal Steriod therapy on the prematurely born infant - a regional MR volumetric and diffusion study

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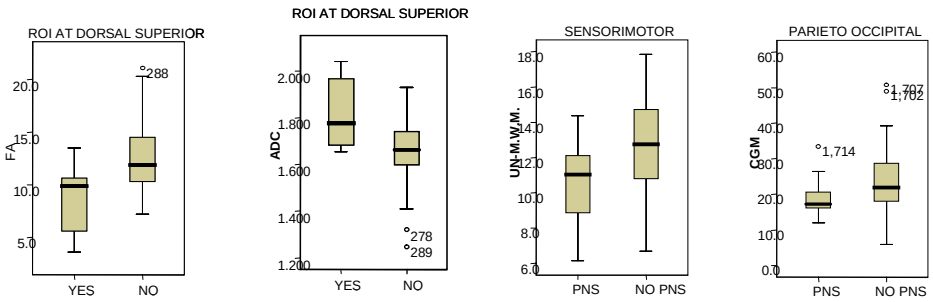
**Introduction**: Perinatal events produce long-term disturbances in cerebral development, and these disturbances can account for cognitive and motor deficits in preterm infants. The tendency for such disturbances may relate to particular vulnerability of actively-developing grey and white matter in the last trimester of human gestation. Very premature infants can suffer from adverse perinatal events, including cardio-respiratory compromise, sepsis and poor nutrition. There is growing evidence that the combination of the insults experienced by the premature brain may be additive in the risk of adverse neurodevelopmental outcome. Bronchopulmonary dysplasia is a recognized risk factor for adverse neurodevelopmental outcome. In addition, the administration of postnatal steroids (PNS) may further increase this risk. Previous data suggested that exposure to postnatal steroids for the premature infant resulted in reduction in cortical gray matter volumes [1]

**Aim**: To investigate the impact of the exposure to postnatal steroids on structural brain development in the premature infant utilizing both diffusion and volumetric magnetic resonance imaging.

**Method:** 3D MRI and advanced image processing algorithms were used to perform quantitative volumetric analysis of 83 preterm infants whose birth weight was less than 1250 g. MRI scans were taken with a 1.5 T GE scanner utilizing a 1.5-mm, SPGR 3D sequence and coronal T2 sequences for primary acquisition. Comparison of regional brain volumes of different tissue classes was performed by dividing the brain into hemispheres and further subdividing each hemisphere into 8 anatomical sectors. Diffusion tensor images were acquired on 43 preterm infant whose weight was less than 1250 g using a line scan protocol (5-6 mm axial slices, 0.5-1 mm gap; TE=78 msec; TR=2139 msec; FOV=22 cm; matrix=256x256; diffusion sensitivity: 2 baselines at b=5 and 6 images at b=700 with diffusion gradients oriented in six non-collinear directions). Quantitative measures of the water apparent diffusion coefficient (ADC) and fractional anisotropy (FA) were calculated from axial images positioned above the lateral ventricles for 6 circular regions of interest (ROI) (area=15 $mm^2$). The data analysis was performed using the SPSS 12.0 linear regression model. The perinatal factors of the presence of sepsis, white and gray matter injury, chronic lung disease, intrauterine growth restriction, administration of antenatal and postnatal steroids , patent ductus arteriosis, and gestational age at birth were taken as independent variables.

**Results:** ***Diffusion imaging***: On multivariate modeling, premature infants who received PNS displayed a significant increase in the frontal region ADC (no PNS 1.664±0.156 $\mu m^2$/ms vs. PNS 1.817±0.158 $\mu m^2$/ms, p=0.007) with a reduction in FA (no PNS 13.5±4.2 vs. PNS 9.0±3.0, p=0.011). ***Conventional MRI***: For premature infants who received PNS, there was no significant change in the tissue volumes in any of 16 parcellated cerebral regions. After separating the analysis for gender, there was a significant reduction in three regions of cortical gray matter volumes, including the right midtemporal region (noPNS 5.7±1.9 $cm^3$ vs. PNS 5.3±2.2 $cm^3$, p=0.04), the left left and right parietoccipital regions (left: noPNS 26.6±7.9 $cm^3$ vs. PNS 22.3±6.9 $cm^3$, p=0.04: right noPNS 23.4±8.2 $cm^3$ vs. PNS 19.2±6.1 $cm^3$, p=0.02). In males who received PNS, unmyelinated white matter volumes were reduced in the left sensorimotor (noPNS 12.6 ±2.8 $cm^3$ vs. PNS 10.5±2.6 $cm^3$, p=0.014) and left midtemporal region (no PNS 6.8 ±2.0 $cm^3$ vs. PNS 6.0±1.2 $cm^3$, p=0.04).




**Conclusion:** Cerebral structural development is altered by premature birth, with regional disturbances in volumetric and diffusion measures, despite controlling for multiple confounding factors. Postnatal steroid exposure in the premature infant resulted in alteration in frontal white matter microstructure. In addition, there was a regional reduction in gray matter and unmyelinated white matter volumes in the male infant. This effect may be related to gender-dependent differences in cerebral receptor populations and/or hormonal milieu. Both premature birth and postnatal steroid exposure alter white matter microstructure and regional brain development in the premature infant.

[1] Brendan P. Murphy, MB BCh, Terrie E.Inder, MD,Petra S. Huppi, MD, Simon Warfield PhD, Gary P. Zientra PhD, Ron Kikins, MD Ferenc A Jolesz, MD, and Joseph J. Volpe, MD, Impaired Cerebral Cortical Gray Matter Growth After Treatment With Dexamethasone for Neonatal Chronic Lung Disease, PEDIATRICS Vol 107 No 2 February 2001, pp 217 -221