September 21st, 2023 11:00 - 12:30

PARALLEL SESSION 14 - LUNG 3

ID 128. Impact of Bronchopulmonary Dysplasia on Brain GABA And Glutamate Concentrations of Preterm Infants

Doctor Sudeepta Basu[1], Kushal Kapse, Emma Spoehr, Jonathan Murnick, Nickie Andescavage, Professor Adre duPlessis, Professor Catherine Limperopoulos

[1]Children's National Hospital/the George Washington University, Washington, United States

Background: Bronchopulmonary dysplasia (BPD) adversely impacts neurodevelopmental outcomes in preterm infants, but the neuropathologic link is not clearly understood. GABA–editing Mescher–Garwood point resolved spectroscopy (MEGA–PRESS) allows in–vivo brain gamma–aminobutyric acid (GABA+, with macromolecules) and glutamate (Glx, with glutamine) concentrations, the principal inhibitory and excitatory neurotransmitters in the developing brain. This technique allows investigation of how BPD disrupts the normal neurosignalling and may lead to neurodevelopmental deficits in preterm infants.
Objective: To investigate relationship of severity of BPD with in–vivo GABA+ and Glx concentrations in the preterm infant's brain at TEA.

Methods: MEGA–PRESS on a 3T scanner were acquired from a prospective cohort of preterm infants born at ⩽32 weeks gestational age (GA) and healthy term infants (>37 weeks GA) at term–equivalent age. A 3cm3 MEGA–PRESS (TE 68ms, TR 2000ms, 256 averages) voxel was placed in the right basal ganglia and water referenced LCModel output was used to quantify metabolites in institutional units

(i.u). Severity of BPD was classified as mild (grade 0 or 1) or moderate–severe (grade 2 or 3) using the 2019 Neonatal Research Network definition.

Results: MEGA–PRESS data was available from 30 term and 37 preterm infants without structural brain injury, acquired at a median postmenstrual age (PMA) of 43 and 40 wks, respectively (Table1). The preterm infants with moderate–severe BPD (n=20) were born at a median 26 wks GA at birth, compared with 29.6 wks ($p<0.001$) for those with mild BPD (Table 1). Infants with moderate–severe BPD had the lowest right basal ganglia GABA+ (median 1.88 i.u.) and N–acetylaspartate (6.09) concentrations and GABA+/Choline ratio (0.73), and highest Choline concentrations compared with other preterm and term infants (Table 1). GABA+/Glx ratio was lower (median 0.34 vs 0.44) in preterm infants with moderate–severe BPD, compared with those with mild BPD. Adjusted for GA at birth and PMA at MRI, differences in GABA+, GABA+/Glx and GABA+/Choline between the infant groups remained statistically significant.

Conclusions: We posit that the lower GABA+ and GABA+/Glx in preterm infants with moderate–severe BPD may indicate early perturbations in the inhibitory/excitatory neurosignalling and may serve as biomarkers of future neurocognitive deficits in preterm infants.

Clinical characteristics	Preterm infants (n=37)		Term infants C (n=30)	ANOVA on Ranks/Chi-square test (A vs B vs C) p value @	ANCOVA adjusted for covariates @@
	Mid BPD (Grade 0/1) A (n=17)	Moderate-Severe BPD (Grade 2/3) B (n=20)			
GA at birth (in weeks)	29.4 (27.7,31.0)	26.0 (24.0,28.1)	**↑39.7 (39.1,40.3)**	**<0.001**	
Birth weight (in grams)	1220 (740,1395)	895 (626,1096)	**↑3345 (3123,3658)**	**<0.001**	
PMA at MRI (in weeks)	39.1 (37.9,4.0)	40.1 (39.1,41.3)	**↑43.6 (42,45.2)**	**<0.001**	
Female Sex	9 (53%)	11 (55%)	14 (47%)	NS	
Afro-American Race	11 (64%)	8 (61%)	11 (36%)	NS	
Vaginal delivery	5 (29%)	8 (42%)	17 (57%)	NS	
Apgar at 5 min	8 (6,9)	8 (7,8)	9 (8,9)	NS	
IVH grade>2	0 (0%)	2 (10%)		NS	
PDA mod_large	6 (35%)	10 (55%)		NS	
NEC	5	8		NS	
Sedation exposure > 1mth of life	7 (42%)	13 (65%)		NS	
Dexamethasone administration	1 (6%)	7 (35%)		0.057	
Right Basal Ganglia Metabolite (in i.u.)					
GABA+	2.20 (1.8,2.9)	**↓1.88 (1.5,2.2)**	2.12 (1.8,2.4)	0.14	**0.013**
Glx	4.52 (3.9,6.2)	5.39 (4.9,6.9)	5.76 (5.2,6.4)	0.19	NS
N-acetylaspartate	6.33 (5.2,6.9)	**↓6.09 (5.4,6.9)**	6.9 (6.2,7.6)	**0.031**	NS
Choline	2.41 (2.3,2.5)	**↑2.68 (2.4,2.8)**	2.35 (2.2,2.5)	**0.004**	0.12
Creatine	6.61 (5.9,7.5)	7.22 (6.7,7.9)	6.83 (6.4,7.5)	0.10	NS
GABA+/Glx	**↑0.44 (0.39,0.54)**	0.34 (0.27,0.42)	0.35 (0.29,0.43)	**0.044**	**0.043**
GABA+/Choline	0.99 (0.86,1.08)	**↓0.73 (0.59,0.87)**	0.87 (0.72,1.02)	**0.005**	**0.008**

Classification of bronchopulmonary dysplasia (BPD) based on severity grades recommended by NRN2019 definition, and further dichotomized as mild (Grade 0 or 1, Column A) and moderate-severe (Grade 2 or 3, Column B)

@ ANOVA on Ranks or Chi-square tests performed to detect group differences between infants in groups A, B, and C.

@@ For significant differences in metabolites, ANCOVA was performed adjusted for GA at birth, PMA at MRI, and dexamethasone administration.

Rank Sum Test was performed for differences in between preterm infants with (gp B) and without (gp A) moderate-severe BPD

↑ or ↓ Indicates highest or lowest metabolite concentration with significant group differences

Clinical characteristics and Basal Ganglia metabolites stratified by prematurity and BPD severity

Clinical characteristics and Basal Ganglia metabolites stratified by prematurity and BPD severity

"None declared"

ID 771. LUNG AND BRAIN PROTECTION IN VLBW INFANTS AFTER ANTENATAL STEROID COURSE: DOES TIMING MATTER?

Flavia Pozzi[1], **Paolo Massirio**[2], Francesco Vinci[2], Irene Bonato[2], Maria Grazia Calevo[3], Dario Paladini[4], Federico Prefumo[5], Mariasavina Severino[6], Domenico Tortora[6], Andrea Rossi[6,7], Diego Minghetti[2], Mrs Mariya Malova[2], Luca Ramengi[2,8]
[1]Single-cycle master degree course in Medicine and Surgery, University of Genoa, Genoa, Italy, [2]Neonatal Intensive Care Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [3]Epidemiology and Biostatistics Unit, Scientific Direction, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [4]Fetal Medicine and Surgery Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [5]Obstetrics and Gynecology Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [6]Neuroradiology Unit, IRCCS Istituto Giannina Gaslini, Genoa, Italy, [7]Department of Health Sciences (DISSAL), University of Genoa, Genoa, Italy, [8]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics and Maternal and Child Health (DINOGMI), University of Genoa, Genoa, Italy

Background: Antenatal corticosteroids (ACS) are widely used in pregnancies at risk of preterm birth to target lung maturation, but their role in brain development is debated. Some studies suggest that protective effect on lung vanishes if more than 7 days has passed between administration and birth. The aim of our study was to evaluate effects of complete course of ACS (ccACS) on lung and brain with attention to timing and with the help of MRI, known to be more sensitive to intraventricular hemorrhage (IVH) than previously used cranial ultrasound (Parodi et al, 2015).

Methods: All VLBW infants admitted to our NICU from January 2019 to December 2021 were included. Clinical data including timing of ACS and respiratory outcome were registered. Term-equivalent age MRI scans were reviewed to identify IVH, white matter lesions (WML), and cerebellar hemorrhage (CBH). Linear measurements of

brain size were carried out and total maturation score was calculated. Lung and brain parameters were compared between infants with and without ccACS, and between subgroups of infants with time between steroid administration and birth being less vs more than 7, 14 and 21 days.

Results: Out of 189 infants included, 139 (73,5%) received ccACS. Infants with ccACS presented higher 5 minutes Apgar score (p=0.001), lower use of surfactant (p=0.005) and a trend for lower rate of intubation (60.4% vs 76%, p=0.06). We have not observed significant reduction of beneficial effect on lungs in infants delivered more than 7, 14 or 21 days after ACS. On MRI infants with ccACS had less WML (p=0.02) and less severe IVH (p=0.04). In the extremely preterm (<28 weeks) subgroup at higher risk of IVH we have observed a significant reduction of IVH in infants receiving ccACS less than 7 days before birth. No significant differences were observed between groups in brain size and maturation.

Conclusion: According to our data, timing of ACS does not matter for the lung protection. Nevertheless, reduction of IVH in extremely preterm infants seems to be more pronounced when less than 7 days has passed from ACS administration to birth. Our study suggests a reduction of WML following ccACS.

None declared