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The association between the ventricle ratio of preterm infants and the motor develpmental delay in childhood

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Early prediction and timely intervention are particularly essential for high-risk preterm infants. Brain magnetic resonance imaging (bMRI) is frequently used alongside functional evaluations to improve predictions of developmental outcomes. This study aimed to assess voxel-based brain volumetry in extremely preterm infants using bMRI at term equivalent age (TEA) and investigate its association with developmental outcomes.

Methods

From March 2016 to December 2019, a retrospective review of medical records was conducted on preterm infants admitted to neonatal intensive care units at CAUH. The study included infants with a gestational age <32 weeks, a birth weight < 1500 g, a bMRI at term equivalent age ± 2 weeks, and a follow-up developmental assessment by Bayley-III.

- **Developmental assessment**

Development was assessed using the Bayley Scales of Infant Development, 3rd edition (BSID-III), administered by an experienced occupational therapist.

The Chung-Ang University Hospital's clinical protocol for the first Bayley assessment follow-up occurs at a corrected age of 8-9 months.

Composite score <85 were classified as delayed motor development (DMD). Others were classified as typical motor development (TMD) group.

- **Structural MRI**

All brain images were acquired using a 3T Philips Achieva scanner with a T1-weighted gradient echo pulse sequence . Structural images were segmented utilizing ITK-SNAP.

T1-weighted MRI scans were visually inspected to exclude significant artifacts. Trained researchers manually traced contours of the brain cortex and labeled the inner area on each sagittal slice. After. labeled volumes were segmented into cerebellum, lateral ventricles, and the remainder. Finally, segments were smoothed with a Gaussian kernel to minimize noise. (Figure 1)

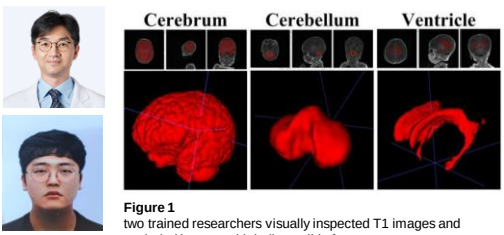

Figure 1
two trained researchers visually inspected T1 images and excluded images with indiscernible features

Results

- **Comparison of Bayley Scales of Infant Development**

Characteristics	TMD (n=38)	DMD (n=9)	Statistics
Bayley age (months)	8.7±4.2	9.5±5.7	z= -1.07, p=0.61
Motor composite score	99.3±15.7	67.4±22.9	z= 5.00, p<0.01
Motor composite delay (n)	0	9	-
Gross motor scale score	9.7±3.3	3.9±4.5	z= 4.48, p<0.01
Gross motor delay (n)	1	7	χ^2=29.1, p<0.01
Fine motor scale score	9.9±2.7	5.1±3.6	z= 4.55, p<0.01
Fine motor delay (n)	1	6	χ^2=23.5, p<0.01
Cognitive composite score	99.8±8.9	81.7±18.9	z= 4.33, p<0.01
Cognition delay (n)	0	2	χ^2=8.8, p=0.03
Language composite score	103.8±9.3	85.1±21.7	z= 4.05, p<0.01
Language delay (n)	0	4	χ^2=18.5, p<0.01

- **Demographic and clinical characteristics of children and mothers**

There were no significant differences in demographic and clinical characteristics between TMD and DMD groups.

- **Comparison of brain parenchyma and ventricle sizes in infants**

Variables	TMD (n=38)	DMD (n=9)	statistics
Cerebrum			
Whole Brain (voxels)	1122267.6±273436.8	692438.0±333398.3	z= -1.71, p=0.09
Right brain (voxels)	560091.1±137446.9	345737.0±169672.7	z= -1.40, p=0.12
Left brain (voxels)	562173.4±136748.6	346701.0±164994.4	z= 1.36, p=0.18
Ventricle			
Whole ventricle (voxels)	6795.9±9244.9	18012.8±27466.7	z= -2.11, p=0.04*
Whole ventricle (ratio, %)	1.1±1.2	2.4±2.9	z= -2.11, p=0.04*
Right ventricle (voxels)	3805.3±5298.2	10579±15347.9	z= -2.27, p=0.03*
Right ventricle (ratio, %)	0.64±0.72	1.44±1.39	z= -2.27, p=0.03*
Left ventricle (voxels)	2992.7±4046.3	7433.6±12163.9	z= -1.90, p=0.06
Left ventricle (ratio, %)	0.47±0.50	0.83±1.28	z= -1.37, p=0.18
Cerebellum			
Whole Cerebellum (voxels)	35635.2±12782.8	47188.9±13325.9	z= -0.95, p= 0.35
Whole Cerebellum (ratio, %)	6.2±1.9	6.4±1.9	z= -0.33, p= 0.75
Right Cerebellum (voxels)	18628.0±17291.8	24218.3±16780.8	z= -0.88, p= 0.39
Right Cerebellum (ratio, %)	3.23±1.10	3.24±0.93	z= -0.47, p= 0.96
Left Cerebellum (voxels)	17007.2±15668.8	22970.6±16744.8	z= -1.01, p= 0.32
Left Cerebellum (ratio, %)	2.92±0.93	3.14±1.06	z= -0.61, p= 0.55

- **Hierarchical logistic regression analysis for motor development delay**

	Model 1				Model 2			
	B	Wald	Sig	OR	B	Wald	Sig	OR
Demographics of infants								
Sex	0.104	0.016	0.898	1.109	-0.524	0.285	0.594	0.592
Gestational age	0.210	3.837	0.050	1.234	0.073	0.238	0.625	1.076
Birth weight	-0.001	1.742	0.187	0.999	-0.001	0.690	0.406	0.999
Clinical status of infants								
APGAR score 1min					0.722	1.621	0.203	2.058
APGAR score 5min					-0.981	1.652	0.199	0.375
RDS					-2.256	2.039	0.153	0.105
BPD					0.574	0.233	0.629	1.776
PDA					2.985	3.870	0.049*	19.783
Other Med Conditions					-0.901	0.587	0.444	0.406
Model Statistics					Model Statistics			
-2LL	39.592				32.163			
Model χ2	χ2 = 5.885, p = 0.117				χ2 = 13.314, p = 0.149			
Step χ2	χ2 = 5.885, p = 0.117				χ2 = 7.429, p = 0.283			
Nagelkerke R^2	0.191				0.400			
Class Accuracy	78.3 %				82.6 %			
	Model 3				Model 4			
Demographics of infants								
Sex	-0.702	0.433	0.511	0.496	0.095	0.001	0.974	1.099
Gestational age	0.076	0.249	0.618	1.078	0.154	0.297	0.586	1.166
Birth weight	0.000	0.295	0.587	1.000	-0.002	1.556	0.212	0.998
Psychological status								
Apga score 1min	0.730	1.582	0.208	2.075	1.649	2.183	0.140	5.200
Apga score 5min	-1.035	1.721	0.190	0.355	-2.709	2.635	0.105	0.067
RDS	-2.409	2.082	0.149	0.090	-3.879	1.128	0.288	0.021
BPD	0.601	0.236	0.627	1.825	-0.119	0.003	0.955	0.888
PDA	2.901	3.370	0.066	18.199	3.542	1.651	0.199	34.522
Other Med Conditions	-0.982	0.628	0.428	0.375	-2.186	0.973	0.324	0.112
Maternal factors								
Age	-0.043	0.247	0.619	0.958	-0.019	0.015	0.904	0.981
Perinatal Diseases	0.280	0.041	0.840	1.323	-1.726	0.671	0.413	0.178
Prenatal Steroid	0.189	0.023	0.880	1.208	3.641	1.630	0.202	38.129
Brain factor								
Ventricle ratio					1.443	4.247	0.039*	4.233
Cerebellum ratio					1.049	1.226	0.268	2.856
Model Statistics					Model Statistics			
-2LL	31.759				20.236			
Model χ2	χ2 = 13.718, p = 0.319				χ2 = 25.241, p=0.03*			
Step χ2	χ2 = 0.404, p = 0.940				χ2 = 11.523, p=0.003*			
Nagelkerke R^2	0.411				0.673			
Class Accuracy	82.6%				99.5%			

Conclusions

This study identified a correlation between reduced brain parenchymal volume and adverse developmental motor outcomes. These findings imply that brain MRI volumetry could serve as a valuable instrument for predicting developmental motor outcomes in preterm infants, enabling early interventions and better long-term outcomes.

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