

Electronic supplementary material (ESM)

Supplementary Table 1. Differences between the study group and the fetuses that were removed from the cohort

Characteristics	Study group	Removed from the cohort	P-value
n	70	16	
Fetal gender			
Male	34 (48.6%)	4 (75%)	0.09
Female	36 (51.4%)	12 (25%)	
Maternal age at birth, years	34.0	30.5	0.36
Length of pregnancy, weeks	38.9	39.1	0.48
MRI 3D biometry			
STV, centile	28.0	12.5	0.41
CV, centile	48.5	38.0	0.99
CV/STV	58.5	82.0	0.22
MRI 2D biometry			
OFD	57.5	50.0	0.57
BPD	40.0	22.5	0.23
TCD	50.0	50.0	0.26

* BPD, bi-parietal diameter; OFD, occipitofrontal diameter; TCD, trans-cerebellar diameter; STV, supratentorial brain volume; CV, cerebellar volume.

** P-value refers to Mann–Whitney U test or Chi-squared test.

Supplementary Table 2. Obstetrical data of the study population

Maternal parameters, median (IQR)	
Gravidity	3 (1-4)
Parity	1 (0-2)
Abortions	0 (0-1)
Maternal diseases, n (%)	
Hypothyroidism	5 (7.1%)
Gestational Diabetes Mellitus	14 (20%)
Diabetes Mellitus type I or II	2 (2.8%)
Anemia	4 (5.7%)
Thrombocytopenia	7 (10%)
Current smoking	2 (2.9%)
Hypertension	1 (1.4%)
Mode of conception, n (%)	
Spontaneous	60 (87%)
In vitro fertilization	7 (10.1%)
Clomiphene Citrate	2 (2.9%)
Mode of delivery, n (%)	
Vaginal birth	41 (59.4%)
Elective cesarean section	16 (23.2%)
Urgent cesarean section	8 (11.6%)
Vacuum extraction	4 (5.8%)
Median birth weight, grams (IQR)	
3,130 (3427-2858)	
5-minute Apgar score < 8	
0 (0%)	
Birth complications, n (%)	
Premature rupture of membranes	3 (4.2%)
Abruptio placentae	1 (1.4%)
Meconium in birth	6 (8.6%)

Supplementary Table 3. Vineland II adaptive behavior scores of the study population.

	N (%)	Mean (SD)
Communication domain, standard score		104.8 (16.6)
Low	1 (1.4%)	
Moderately low	7 (10.0%)	
Adequate	43 (61.4%)	
Moderately high	13 (18.6%)	
High	6 (8.6%)	
Daily living skills domain, standard score		99.6 (13.5)
Low	1 (1.4%)	
Moderately low	8 (11.4%)	
Adequate	51 (72.9%)	
Moderately high	10 (14.3%)	
High	0 (0%)	
Socialization domain, standard score		96.9 (11.5)
Low	1 (1.4%)	
Moderately low	9 (12.9%)	
Adequate	55 (78.6%)	
Moderately high	5 (7.1%)	
High	0 (0.0%)	
Motor skills domain, standard score		99.3 (17.2)
Low	2 (3.5%)	
Moderately low	9 (15.8%)	
Adequate	36 (63.2%)	
Moderately high	7 (12.3%)	
High	3 (5.3%)	
Adaptive behavior composite standard score		99.8 (13.8)
Low	1 (1.4%)	
Moderately low	8 (11.4%)	
Adequate	51 (72.9%)	
Moderately high	10 (14.3%)	
High	0 (0.0%)	

Supplementary Table 4. Comparison of median (IQR) Vineland-II adaptive behavior scores between microcephalic and normal fetuses according to 2D and 3D fetal brain MRI biometry.

Percentile of biometric value	4-96	≤3	p-value
MRI 2D OFD , number of fetuses	58	1	
Communication domain standard score	105 (116-94)	125	n/a
Daily living skills domain standard	101 (109-92)	97	n/a
Socialization domain standard score	96 (105-89)	108	n/a
Motor skills domain standard score	100 (114-89)	94	n/a
MRI 2D BPD , number of fetuses	61	6	
Communication domain standard score	104 (115-93)	108 (122-97)	0.51
Daily living skills domain standard	100 (109-91)	100 (110-94)	0.72
Socialization domain standard score	96 (105-89)	98 (106-85)	1.0
Motor skills domain standard score	100 (114-88)	100 (108-91)	0.91
MRI 2D TCD , number of fetuses	69	0	
Adaptive behavior composite standard score	99 (110-90)		n/a
Communication domain standard score	106 (116-94)		n/a
Daily living skills domain standard	100 (108-91)		n/a
Socialization domain standard score	96 (105-88)		n/a
Motor skills domain standard score	100 (112-88)		n/a
MRI 3D STV , number of fetuses	43	16	
Communication domain standard score	104 (116-95)	105 (124-94)	0.6
Daily living skills domain standard	99 (107-93)	105 (115-92)	0.28
Socialization domain standard score	95 (103-88)	104 (106-90)	0.32
Motor skills domain standard score	100 (106-92)	102 (116-87)	0.53
MRI 3D CV , number of fetuses	53	9	
Communication domain standard score	106 (117-96)	104 (119-84)	0.44
Daily living skills domain standard	100 (109-93)	104 (117-82)	0.76
Socialization domain standard score	96 (105-89)	91 (107-86)	0.91
Motor skills domain standard score	100 (111-88)	100 (114-88)	0.68
MRI 3D CV/STV ratio , number of fetuses	58	1	
Adaptive behavior composite standard score	98 (109-89)	109	n/a
Communication domain standard score	103 (114-93)	116	n/a
Daily living skills domain standard	98 (107-91)	118	n/a
Socialization domain standard score	95 (105-89)	107	n/a
Motor skills domain standard score	97 (104-88)	88	n/a

* BPD, bi-parietal diameter; OFD, occipitofrontal diameter; TCD, trans-cerebellar diameter; STV, supratentorial brain volume; CV, cerebellar volume.

** Continuous variables are presented as median (interquartile range).

*** P-value refers to Mann–Whitney U test.

Supplementary Table 5. Comparison of median (IQR) Vineland-II adaptive behavior scores between macrocephalic and normal fetuses according to 2D and 3D fetal brain MRI biometry.

Percentile of biometric value	4-96	≥97	p-value
MRI 2D OFD , number of fetuses	58	11	
Communication domain standard score	105 (116-94)	95 (113-91)	0.31
Daily living skills domain standard	101 (109-92)	93 (102-88)	0.15
Socialization domain standard score	96 (105-89)	92 (102-88)	0.45
Motor skills domain standard score	100 (114-89)	91 (100-83)	0.15
MRI 2D BPD , number of fetuses	61	3	
Communication domain standard score	104 (115-93)	115	0.65
Daily living skills domain standard	100 (109-91)	97	0.88
Socialization domain standard score	96 (105-89)	90	0.95
Motor skills domain standard score	100 (114-88)	81	0.23
MRI 2D TCD , number of fetuses	69	1	
Adaptive behavior composite standard score	99 (110-90)	86	n/a
Communication domain standard score	106 (116-94)	91	n/a
Daily living skills domain standard	100 (108-91)	93	n/a
Socialization domain standard score	96 (105-88)	90	n/a
Motor skills domain standard score	100 (112-88)	81	n/a
MRI 3D STV , number of fetuses	43	11	
Communication domain standard score	104 (116-95)	106 (108-91)	0.28
Daily living skills domain standard	99 (107-93)	93 (100-83)	0.11
Socialization domain standard score	95 (103-88)	97 (105-88)	0.98
Motor skills domain standard score	100 (106-92)	94 (108-82)	0.28
MRI 3D CV , number of fetuses	53	8	
Communication domain standard score	106 (117-96)	99 (107-92)	0.2
Daily living skills domain standard	100 (109-93)	96 (102-85)	0.15
Socialization domain standard score	96 (105-89)	93 (103-88)	0.51
Motor skills domain standard score	100 (111-88)	94 (114-84)	0.53
MRI 3D CV/STV ratio , number of fetuses	58	11	
Adaptive behavior composite standard score	98 (109-89)	103 (125-91)	0.13
Communication domain standard score	103 (114-93)	109 (132-94)	0.24
Daily living skills domain standard	98 (107-91)	107 (111-95)	0.13
Socialization domain standard score	95 (105-89)	103 (106-88)	0.44
Motor skills domain standard score	97 (104-88)	104 (121-88)	0.19

* BPD, bi-parietal diameter; OFD, occipitofrontal diameter; TCD, trans-cerebellar diameter; STV, supratentorial brain volume; CV, cerebellar volume.

** Continuous variables are presented as median (interquartile range).

*** P-value refers to Mann–Whitney U test.

Supplementary Table 6. Correlation among 2D and 3D MRI fetal head biometry and Vineland-II adaptive behavior standard scores.

	Correlation coefficient	p-value	adjusted p-value
MRI 2D OFD and			
Communication domain standard score	-0.16	0.18	0.425
Daily living skills domain standard score	-0.21	0.09	0.277
Socialization domain standard score	-0.08	0.49	0.613
Motor skills domain standard score	-0.13	0.35	0.543
Adaptive behavior standard score	-0.16	0.2	0.431
MRI 2D BPD and			
Communication domain standard score	-0.15	0.22	0.438
Daily living skills domain standard score	-0.31	0.01	0.105
Socialization domain standard score	-0.12	0.31	0.538
Motor skills domain standard score	-0.12	0.39	0.543
Adaptive behavior standard score	-0.20	0.1	0.277
MRI 2D TCD and			
Communication domain standard score	0.025	0.84	0.840
Daily living skills domain standard score	-0.185	0.12	0.325
Socialization domain standard score	-0.052	0.67	0.764
Motor skills domain standard score	0.56	0.68	0.764
Adaptive behavior standard score	-0.042	0.73	0.801
MRI 3D STV and			
Communication domain standard score	-0.183	0.13	0.325
Daily living skills domain standard score	-0.260	0.03	0.188
Socialization domain standard score	-0.147	0.23	0.438
Motor skills domain standard score	-0.117	0.39	0.543
Adaptive behavior standard score	-0.203	0.09	0.277
MRI 3D CV and			
Communication domain standard score	-0.103	0.4	0.543
Daily living skills domain standard score	-0.121	0.32	0.538
Socialization domain standard score	-0.031	0.8	0.825
Motor skills domain standard score	-0.040	0.77	0.814
Adaptive behavior standard score	-0.077	0.53	0.637
MRI 3D CV/STV and			
Communication domain standard score	0.091	0.45	0.586
Daily living skills domain standard score	0.242	0.04	0.188
Socialization domain standard score	0.120	0.32	0.538
Motor skills domain standard score	0.269	0.04	0.188
Adaptive behavior standard score	0.221	0.06	0.257

* BPD, bi-parietal diameter; OFD, occipitofrontal diameter; TCD, trans-cerebellar diameter; STV, supratentorial brain volume; CV, cerebellar volume.

** p-value was adjusted for multiple comparisons using the Benjamini–Hochberg procedure.

Supplementary Table 7. Intraclass correlation coefficients and confidence interval for interobserver and intraobserver measurements:

Structure measured	Interobserver		Intraobserver	
	ICC	95% Confidence interval	ICC	95% Confidence interval
STV	0.851	0.467-0.962	0.98	0.922-0.995
CV	0.742	0.09-0.935	0.923	0.727-0.980

* STV, supratentorial brain volume; CV, cerebellar volume; ICC, intraclass correlation coefficient.