Impact of Neonatal Growth on IQ and Behavior at Early School Age

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KEY WORDS

neonatal growth, weight gain, head circumference, IQ, behavior

ABBREVIATIONS

CI—confidence interval

FSIQ—full-scale IQ

HCG—neonatal gain in head circumference

NWG—neonatal weight gain

PIQ—performance IQ

PROBIT—Promotion of Breastfeeding Intervention Trial

SDQ—Strengths and Difficulties Questionnaire

VIQ—verbal IQ

WASI—Wechsler Abbreviated Scale of Intelligence

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WHAT'S KNOWN ON THIS SUBJECT: Feeding difficulties often emerge during the neonatal period and affect neonatal growth. Growth throughout the first years of life is associated with children's IQ scores and risk of behavioral problems.

WHAT THIS STUDY ADDS: Among infants born full term (≥ 37 weeks' gestation) with birth weight ≥ 2500 g, gain in weight and head circumference during the neonatal period is associated with higher IQ, but not with behavior at 6.5 years of age.

abstract

OBJECTIVES: The objective was to examine associations of neonatal weight gain (NWG) and head circumference gain (HCG) with IQ scores and behavior at early school age.

METHODS: We used data from the Promotion of Breastfeeding Intervention Trial, involving Belarusian infants born full term and weighing ≥ 2500 g. NWG and HCG were measured as the percentage gain in weight and head circumference over the first 4 weeks relative to birth size. IQ and behavior were measured at 6.5 years of age by using the Wechsler Abbreviated Scales of Intelligence and the Strengths and Difficulties Questionnaire (SDQ), respectively, with SDQ collected from parents and teachers. The associations between the exposures (NWG, HCG) and children's IQ and SDQ were examined by using mixed models to account for clustering of measurements, and adjustment for potentially confounding perinatal and socioeconomic factors.

RESULTS: Mean NWG was 26% (SD 10%) of birth weight. In fully adjusted models, infants in the highest versus lowest quartile of NWG had 1.5-point (95% confidence interval [CI] 0.8 to 2.2) higher IQ scores ($n = 13\,840$). A weak negative (protective) association between NWG and SDQ total difficulties scores was observed for the teacher-reported ($\beta = -0.39$, 95% CI -0.71 to -0.08 , $n = 12\,016$), but not the parent-reported ($\beta = -0.12$, 95% CI -0.39 to 0.15 , $n = 13\,815$), SDQ. Similar associations were observed with HCG and IQ and behavior.

CONCLUSIONS: Faster gains in weight or head circumference in the 4 weeks after birth may contribute to children's IQ, but reverse causality (brain function affects neonatal growth) cannot be excluded. *Pediatrics* 2013;132:e53–e60

The neonatal period is a time when the mother and her infant establish feeding patterns. Feeding difficulties often emerge during the neonatal period and are a common reason for hospitalization.¹ Feeding difficulties can influence infant growth, and anthropometric measurements, such as weight, length, and head circumference, are routinely monitored to ensure infants are growing appropriately. At the extreme, infants with feeding difficulties may be diagnosed with growth faltering (or “failure to thrive”), which has been associated with 3- to 4-point lower IQ scores compared with children without growth faltering.^{2,3}

Previous studies in nonclinical populations suggest that faster growth in infancy and childhood is associated with better cognitive outcomes,^{4–8} although some findings have been null.⁹ Disparities in the literature may reflect varying methods of analysis, small sample sizes (resulting in insufficient statistical power), and differences in the age period studied. Studies of children examined over many years suggest that growth in the first year is more important for children's cognitive and behavioral outcomes than growth after 1 year.^{7,8} Although the first few months of life appear important, we are unaware of any studies of nonclinical samples that examine links between growth during the neonatal period and children's cognitive development.

The aim of this study was to examine whether weight gain during the neonatal period is associated with cognitive and behavioral outcomes in childhood, using data collected from a large sample of healthy, term-born infants with a broad spectrum of neonatal growth. In parallel analyses, we investigated the association between brain growth during the neonatal period (as indicated by gain in head circumference) and children's cognitive

or behavioral outcomes. We separately examined gains in weight and head circumference, because these measurements may be indicative of different underlying growth processes.

METHODS

The Promotion of Breastfeeding Intervention Trial (PROBIT) is a cluster-randomized controlled trial of a breastfeeding intervention that is based on the World Health Organization's Baby-Friendly Hospital Initiative. Details of PROBIT have been previously published.¹⁰ Briefly, participants were 17 046 mothers and their healthy singleton infants born at ≥ 37 weeks' gestation and weighing ≥ 2500 g during 1996 to 1997 in Belarus. The current study was conducted on the children who had anthropometric measurements at 1 month, all relevant covariables, and follow-up assessments of IQ or behavior at 6.5 years of age. PROBIT was approved by the institutional review board of the Montreal Children's Hospital, and signed consent in Russian was obtained from the accompanying parent.

Exposures

Birth weight and head circumference were extracted from maternity hospital birth records. At 1 month of age, weight and head circumference were measured at a planned follow-up visit with trial pediatricians. Neonatal weight gain (NWG) was calculated as the gain in weight between birth and 1 month of age, divided by birth weight, and multiplied by 100%, that is, as a percentage of birth weight. Neonatal gain in head circumference (HCG) was similarly calculated as the gain in head circumference from birth to 1 month, divided by birth head circumference, and multiplied by 100%. NWG and HCG were categorized into quartiles to avoid the assumption of a linear association with IQ or behavior. The lowest quartile,

which reflects the lowest relative gain in weight or head circumference during the neonatal period, was designated the reference group.

IQ and Behavior Outcomes

Cognitive ability was measured by using the Wechsler Abbreviated Scales of Intelligence (WASI) at 6.5 years.¹¹ The WASI was translated from English to Russian and back-translated to ensure comparability of the Russian version. The WASI was administered by pediatricians who had undertaken extensive training and monitoring by child psychologists and psychiatrists. The vocabulary and similarities subtests of the WASI were used to measure verbal IQ (VIQ), and the block design and matrix reasoning subtests were used to measure performance IQ (PIQ). Raw subtest scores were converted to age- and gender-standardized scores. Children's performance on the verbal and performance domains were combined to yield full-scale IQ (FSIQ) scores.

Child behavior was measured by using the Strengths and Difficulties Questionnaire (SDQ).¹² The SDQ is a behavioral screening questionnaire for 4- to 16-year-old children. The SDQ consists of 5 subscales: emotional symptoms, hyperactivity, conduct problems, peer problems, and prosocial behavior. Each subscale includes 5 questions with 3 possible responses: not true (assigned value of 0), somewhat true (1), or certainly true (2). Scores for each subscale are summed to a total ranging from 0 to 10. The total difficulties score is calculated by summing scores on the emotional symptoms, hyperactivity, conduct problems, and peer problems subscales. Problem behavior is indicated by higher scores on these 4 subscales and the overall total difficulties score, and by lower scores on the prosocial behavior subscale. The SDQ has validity in cross-cultural

settings and for diagnoses of mental health problems in children in clinical and research settings.^{13,14}

The SDQ was completed by both parents and teachers. The parent (usually the mother) who attended the 6.5-year-old PROBIT follow-up clinic with the child completed the SDQ while in the waiting room. Parents of children who had already commenced school provided the teacher's name, and the pediatrician sent the SDQ to the teacher for completion. Of the children who attended the 6.5-year follow-up, the SDQ was completed by 87% of teachers ($n = 12\,016$). The reason for most missing teacher-completed SDQ forms was because the child had not yet commenced school.

Covariables

Potential confounding factors were selected a priori for their potential to influence infant feeding, postnatal growth, IQ, and behavior. Covariables collected at enrollment from mothers included maternal smoking during pregnancy, both parents' education and occupation, area of residence, and number of older siblings. Parental education was categorized as university degree (referent category), partial university, completed secondary, or incomplete secondary. Maternal occupation was categorized as manual (referent), service worker, housewife, or student/unemployed. Paternal occupation was categorized as manual (referent), service worker, farmer, or student/unemployed/unknown. Area of residence was divided into the 4 strata based on rural versus urban, and eastern versus western Belarus. The number of older siblings was categorized into none (referent), 1, or ≥ 2 .

The following covariables were obtained from maternity hospital birth records: gender, gestational age, weight and head circumference at birth, complications during delivery, complications in the

postpartum period, cesarean delivery, 5-minute Apgar scores, and randomized intervention group (breastfeeding promotion or control). Gestational age at birth was based on ultrasound dating (93.9% of children), maternal report of last menstrual period (3.8%), and other obstetric and/or pediatric clinical estimates (2.3%).

Covariables obtained from the 1-month clinic assessments included age (days) and measurements of weight and head circumference. Age at measurement of IQ was not included because the WASI is standardized for age.

Analysis

Gestational age at birth was analyzed as a categorical variable in 1-week units ranging from 37 to 43 completed weeks, with 40 weeks used as the referent category. Birth weight and gestational age are highly collinear, where lower birth weight is associated with faster NWG (regression to the mean). To control for potential confounding by both variables and to avoid problems with collinearity, we calculated birth weight-for-gestational age z-scores (divided into quartiles). Treatment group and breastfeeding are also collinear.¹⁰ Substituting breastfeeding for treatment group resulted in similar findings (data not shown); however, in this study, we control for treatment group to be consistent with previous PROBIT analyses. Across quartiles of NWG, baseline covariables were compared by using the χ^2 test for categorical variables and analysis of variance for continuous variables.

The associations between NWG with IQ and behavior were examined by using mixed models to account for the clustering of measurement by polyclinic for the IQ and parent-reported SDQ outcomes, and for polyclinic and teacher for teacher-reported SDQ. Primary outcomes were FSIQ and SDQ total difficulties scores; secondary outcomes

were subscale scores of the WASI and the SDQ. The first model included NWG in quartiles and adjustment for clustering, whereas the second model included further adjustment for covariables. Because of gender differences in body size, IQ, and SDQ scores, we also examined associations within gender strata. We carried out multiple imputation for missing data to explore attrition bias. Five datasets were created and coefficients were combined according to Rubin's rules.¹⁵

In parallel analyses, we also examined the association between HCG with IQ and SDQ. NWG and HCG were not modeled at the same time because HCG may be a causal intermediate between NWG and outcome, and therefore adjustment for HCG may introduce bias.¹⁶ Statistical analyses were conducted by using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

NWG was calculable in 16 692 (98%) of the 17 046 children enrolled in PROBIT. The number of children with complete NWG, all covariables, and outcome measured was 13 480 (79%) for IQ, 13 815 (81%) for parent-reported SDQ, and 12 016 (70%) for teacher-reported SDQ.

NWG was approximately normally distributed with a mean (SD) of 0.26 (0.10), indicating that, on average, weight gain over the first month was 26% of birth weight. Table 1 shows characteristics of the study sample according to quartiles of NWG.

Neonatal Weight Gain and IQ

The associations between quartiles of NWG and IQ scores are shown in Table 2. Model 1 indicates that after adjustment for clustering, children in the highest quartile of NWG had 0.9 (95% CI 0.2 to 1.5) higher FSIQ scores at 6.5 years compared with children in the lowest quartile, and this association appeared

TABLE 1 Characteristics of Study Sample According to Quartile of NWG (*n* = 13 726)

	Quartiles of NWG								<i>P</i> ^a
	Q1 (lowest)		Q2		Q3		Q4 (highest)		
	<i>n</i> = 3321		<i>n</i> = 3590		<i>n</i> = 3410		<i>n</i> = 3405		
	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	
NWG, mean, SD	0.15	0.04	0.22	0.02	0.28	0.02	0.39	0.07	<.001
Maternal age, y	25.0	5.1	24.6	4.9	24.3	4.8	24.1	4.8	<.001
Maternal education									.14
Completed university	483	14.5	455	12.7	435	12.8	440	12.9	
Partial university	1629	49.1	1861	51.8	1744	51.1	1778	52.2	
Secondary	1089	32.8	1129	31.5	1112	32.6	1067	31.3	
Incomplete secondary	120	3.6	145	4.0	119	3.5	120	3.5	
Maternal occupation									<.001
Manual work	1175	25.3	1271	35.4	1115	32.7	1081	31.8	
Service work	1464	24.5	1561	43.5	1461	42.8	1486	43.6	
Student/unemployed	318	20.6	364	10.1	417	12.2	443	13.0	
Housewife	365	23.2	394	11.0	417	12.2	395	11.6	
Paternal education									.03
Completed university	422	13.1	433	12.5	429	13.0	414	12.7	
Partial university	1493	46.4	1655	47.6	1556	47.1	1605	49.1	
Secondary	1239	38.5	1276	36.7	1243	37.7	1179	36.0	
Incomplete secondary	61	1.9	110	3.2	73	2.2	74	2.3	
Paternal occupation									<.001
Manual work	1454	43.8	1589	44.3	1541	45.2	1578	46.3	
Service work	932	28.1	995	27.7	934	27.4	972	28.6	
Farmer	374	11.3	413	11.5	325	9.5	197	5.8	
Student/unemployed	561	16.9	593	16.5	610	17.9	658	19.3	
Residence									<.001
East, urban	972	29.3	957	26.7	1110	32.6	1408	41.4	
East, rural	624	18.8	636	17.7	536	15.7	433	12.7	
West, urban	738	22.2	864	24.1	839	24.6	843	24.8	
West, rural	987	29.7	1133	31.6	925	27.1	721	21.2	
Maternal smoking during pregnancy									.02
Yes	61	1.8	62	1.7	73	2.1	92	2.7	
No	3260	98.2	3528	98.3	3337	97.9	3313	97.3	
Delivery complications									.20
No	3029	91.2	3285	91.5	3144	92.2	3148	92.5	
Yes	292	8.8	305	8.5	266	7.8	257	7.5	
Cesarean delivery									<.001
No	2837	85.4	3183	88.7	3034	89.0	3102	91.1	
Yes	484	14.6	407	11.3	376	11.0	303	8.9	
Postpartum complications									.33
No	3090	93.0	3359	93.6	3210	94.1	3182	93.5	
Yes	231	7.0	231	6.4	200	5.9	223	6.5	
Older siblings									<.001
None	1760	53.0	1943	54.1	1979	58.0	2085	61.2	
One	1189	35.8	1287	35.9	1167	34.2	1122	33.0	
Two or more	372	11.2	360	10.0	264	7.7	198	5.8	
Child's gender									<.001
Male	1642	49.4	1782	49.6	1768	51.8	1906	56.0	
Female	1679	50.6	1808	50.4	1642	48.2	1499	44.0	
Apgar score at 5 min	8.5	0.7	8.6	0.7	8.6	0.6	8.6	0.6	<.001
Gestational age at birth, wk	39.5	1.0	39.4	1.0	39.4	1.0	39.2	1.0	<.001
Gestational age categories ^a									
37	80	2.4	112	3.1	114	3.3	159	4.7	<.001
38	433	13.0	480	13.4	535	15.7	636	18.7	
39	936	28.2	1099	30.6	1039	30.5	1092	32.1	
40	1556	46.9	1579	44.0	1473	43.2	1312	38.5	
41	257	7.7	266	7.4	207	6.1	181	5.3	
42	56	1.7	51	1.4	39	1.1	24	0.7	
43	3	0.1	3	0.1	3	0.1	1	0.01	

TABLE 1 Continued

	Quartiles of NWG								<i>P</i> ^a
	Q1 (lowest)		Q2		Q3		Q4 (highest)		
	<i>n</i> = 3321		<i>n</i> = 3590		<i>n</i> = 3410		<i>n</i> = 3405		
	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	Mean or <i>n</i>	SD or %	
Birth weight, g	3666	422	3503	383	3379	371	3217	372	<.001
Birth weight–for-GA z-score	0.43	0.90	0.08	0.82	−0.19	0.79	−0.52	0.79	<.001
Categories of birth weight–for-GA z-score ^a									
Q1	329	9.9	611	17.0	957	28.1	1497	44.0	<.001
Q2	634	19.1	958	26.7	939	27.5	928	27.3	
Q3	899	27.1	987	27.5	865	25.4	665	19.5	
Q4	1459	43.9	1034	28.8	649	19.0	315	9.3	
Weight at 1 mo, g	4214	483	4282	467	4333	478	4481	523	<.001
Head circumference at 1 mo, cm	37.2	1.4	37.1	1.4	37.1	1.5	37.2	1.5	<.001
HCG, mean, SD	0.05	0.04	0.06	0.04	0.06	0.04	0.08	0.04	<.001
Categories of HCG ^a									
HCG Q1	1224	37.0	1059	29.5	759	22.3	522	15.4	<.001
HCG Q2	1078	32.5	1220	34.0	1098	32.3	897	26.4	
HCG Q3	418	12.6	529	14.8	640	18.8	625	18.4	
HCG Q4	593	17.9	779	21.7	904	26.6	1348	39.7	
Age at outcome measurement, y	6.6	0.3	6.6	0.3	6.6	0.3	6.6	0.3	.348

GA, gestational age at birth; Q, quartile.

^a Indicates a significant difference in baseline covariables across quartiles in using χ^2 tests for categorical variables and analysis of variance for continuous variables.

to be driven more by VIQ (0.9, 95% CI 0.2 to 1.6) than PIQ (0.6, 95% CI −0.1 to 1.2). Model 2 shows that the positive association between NWG and IQ nearly doubled after adjustment for potentially confounding factors (FSIQ; 1.5, 95% CI 0.8 to 2.2). The imputed analyses yielded results similar to those of the complete case analyses; adjusted analysis comparing the highest with lowest quartile of NWG: FSIQ 1.5 (95% CI 0.8 to 2.2), PIQ 1.0 (95% CI 0.3 to 1.7)

and VIQ 1.6 (95% CI 0.9 to 2.3). The associations between NWG and FSIQ were similar within gender strata (highest compared with lowest quartile of NWG: female 1.5, 95% CI 0.5 to 2.4, male 1.5, 95% CI 0.6 to 2.5).

NWG and Behavior

The associations between NWG and scores on the SDQ are shown in Table 3. The associations differed for the parent- and teacher-completed SDQs. No significant

association was observed between NWG and the parent-completed SDQ total difficulties or any other SDQ subscales. For the teacher-completed SDQ, higher NWG was associated with lower scores for total difficulties (highest compared with the lowest quartile of NWG was −0.39, 95% CI −0.71 to −0.08), emotional symptoms (−0.13, 95% CI −0.24 to −0.02), and peer problems subscales (−0.11, 95% CI −0.21 to −0.02), although the magnitude of the effect was small. These results were consistent with those of the imputed analyses; adjusted analysis comparing SDQ total difficulties in the highest with lowest quartile of NWG: parent-completed SDQ −0.11 (95% CI −0.37 to 0.15) and teacher-completed SDQ −0.39 (95% CI −0.70 to −0.07). Analyses of NWG and SDQ within gender subgroups were also consistent with the main findings (data not shown).

Parallel Analysis: HCG, IQ, and SDQ

Consistent with the findings for NWG, HCG was positively associated with IQ. For example, in fully adjusted models, infants in the highest compared with the lowest quartile of HCG had higher

TABLE 2 Associations Between Quartiles of NWG and IQ at 6.5 y (*n* = 13 840)

	FSIQ		PIQ		VIQ	
	β	95% CI	β	95% CI	β	95% CI
Model 1 (adjusted for clustering of measurement) ^a						
Q1	Referent category					
Q2	−0.2	−0.4 to 0.8	−0.2	−0.8 to 0.5	−0.2	−0.8 to 0.5
Q3	0.1	−0.6 to 0.8	−0.2	−0.8 to 0.5	0.3	−0.3 to 1.0
Q4	0.9	0.2 to 1.5	0.6	−0.1 to 1.2	0.9	0.2 to 1.6
Model 2 (model 1+ adjustment for covariables) ^a						
Q1	Referent category					
Q2	0.2	−0.4 to 0.8	0.1	−0.5 to 0.8	0.2	−0.4 to 0.9
Q3	0.6	−0.03 to 1.3	0.2	−0.4 to 0.9	0.9	0.2 to 1.6
Q4	1.5	0.8 to 2.2	1.0	0.3 to 1.7	1.6	0.9 to 2.4

Q, quartile.

^a Model 1 (base model) includes clustering for polyclinic using mixed models. Model 2 includes clustering by polyclinic (ie, model 1) and covariate adjustment for age at measurement of weight, gender, residential strata, maternal and paternal education and occupation, maternal smoking during pregnancy, 5-min Apgar scores, complications during delivery and the postpartum period, cesarean delivery, older siblings, and treatment group.

TABLE 3 Associations Between Quartiles of NWG and Behavior Problems at 6.5 y^a

	Parent Completed (n = 13 815)		Teacher Completed (n = 12 016)	
	β	95% CI	β	95% CI
Total difficulties				
Q1	Referent		Referent	
Q2	−0.16	−0.40 to 0.08	−0.31	−0.60 to −0.03
Q3	−0.15	−0.40 to 0.09	−0.42	−0.72 to −0.13
Q4	−0.12	−0.39 to 0.15	−0.39	−0.71 to −0.08
Conduct				
Q1	Referent		Referent	
Q2	−0.04	−0.11 to 0.03	−0.05	−0.14 to 0.04
Q3	−0.01	−0.09 to 0.06	−0.06	−0.15 to 0.03
Q4	−0.03	−0.11 to 0.05	−0.06	−0.15 to 0.04
Hyperactivity				
Q1	Referent		Referent	
Q2	−0.03	−0.14 to 0.07	−0.04	−0.17 to 0.09
Q3	−0.12	−0.23 to −0.01	−0.12	−0.26 to 0.02
Q4	−0.03	−0.15 to 0.08	−0.09	−0.23 to 0.06
Emotional				
Q1	Referent		Referent	
Q2	−0.04	−0.14 to 0.06	−0.12	−0.21 to −0.02
Q3	0.04	−0.07 to 0.14	−0.10	−0.20 to 0.002
Q4	−0.03	−0.14 to 0.08	−0.13	−0.24 to −0.02
Peer problems				
Q1	Referent		Referent	
Q2	−0.05	−0.12 to 0.03	−0.11	−0.19 to −0.02
Q3	−0.06	−0.14 to 0.03	−0.15	−0.24 to −0.06
Q4	−0.02	−0.11 to 0.07	−0.11	−0.21 to −0.02
Prosocial				
Q1	Referent		Referent	
Q2	0.01	−0.07 to 0.09	0.03	−0.08 to 0.14
Q3	0.05	−0.03 to 0.14	0.06	−0.05 to 0.17
Q4	0.09	−0.001 to 0.17	0.05	−0.07 to 0.17

^a Analysis includes mixed models to account for clustering by polyclinic (parent-completed SDQ) and for center and teacher (teacher-completed SDQ), and covariable adjustment for age at measurement of weight, gender, residential strata, maternal and paternal education and occupation, maternal smoking during pregnancy, 5-min Apgar scores, complications during delivery and the postpartum period, cesarean delivery, older siblings, and treatment group.

FSIQ (1.5, 95% CI 0.9 to 2.2), PIQ (1.5, 95% CI 0.8 to 2.2), and VIQ (1.3, 95% CI 0.6 to 1.9). No clear association was observed between HCG and children's behavior for either the parent- or teacher-completed SDQ (adjusted models, quartile 4 compared with quartile 1 for total difficulties: parent −0.16, 95% CI −0.41 to 0.10; and teacher −0.26, 95% CI −0.56 to 0.04).

DISCUSSION

We attempted to separate the effect of neonatal growth on childhood cognition and behavior from the effect of other neonatal factors known to contribute to IQ, such as birth weight and gestational age. We found a dose-response relationship between NWG and IQ at 6.5 years of age, with children in the highest

quartile of NWG having 1.5-point (95% CI 0.8 to 2.2) higher FSIQ scores than children in the lowest quartile, which was consistent across gender strata and imputed analyses. These effects were present for VIQ and PIQ subscales, but appeared to be more prominent for VIQ. This is consistent with other literature on the association between early postnatal diet and IQ,^{17,18} and may be attributable to neural structures involved in VIQ developing earlier in life, compared with more protracted development of structures involved in PIQ.¹⁹ Although the direction of the association suggests that higher NWG was linked to fewer difficulties on the SDQ, the magnitude of the associations was small. Furthermore, inconsistencies

according to whether the SDQ was completed by the child's parent or teacher suggest the need for cautious interpretation.

Adjustment for covariates in model 2 strengthened the association between NWG and IQ. We observed the phenomenon of regression to the mean, whereby children with the lowest birth weight-for-gestational age had faster NWG. This phenomenon has been described by Cole,²⁰ who constructed conditional weight gain reference charts to define atypical growth by comparing an infant's current weight against what was predicted from previous weight measurements. Our analysis is conditional on the child's birth weight-for-gestational age z-scores and gestational age at birth. This accounts for regression to the mean, as within each category of gestational age and birth weight-for-gestational age z-scores, children who grew faster had higher IQ scores. According to the developmental origins of disease hypothesis, faster weight gain is linked to poorer long-term health, including greater insulin resistance, obesity, and higher blood pressure.^{21–24} In contrast, our study suggests that greater weight gain, at least during the first month, has advantages for later cognitive ability.

We included the parallel analysis of HCG because different growth processes may underlie gains in head circumference versus weight. Head circumference is an indicator of brain volume.²⁵ A greater increase in neonatal head circumference suggests more rapid brain growth, whereas NWG measures overall growth in body mass. Similar associations were observed between NWG or HCG and IQ, which supports the concept that greater brain growth contributes to higher IQ scores. However, head circumference has greater measurement error than weight, particularly in the few days after birth, as molding resolves.^{26,27} The link between

head size and child development found here is consistent with other studies that examined ultrasound-estimated head size during gestation, at birth, and in the postnatal period. However, some studies have not accounted for factors such as gestational age and weight at birth, and most examined the change in head circumference over the first year rather than the first month.^{7,28}

Studies of postnatal growth and cognitive or behavioral outcomes have focused on weight gain in the first 5 to 12 months of life, not specifically in the neonatal period.^{4–8} In general, more rapid postnatal growth among healthy term-born children is linked to better cognitive outcomes. In one of the few studies that explored the early postnatal period, Emond et al³ showed that children with the lowest 5% of weight gain from birth to 8 weeks had ~3-point lower IQ scores than the rest of the cohort ($n = 7975$). Furthermore, Emond et al³ and others²⁹ indicated that weight gain in the first 1 to 2 months after birth is more important for later development than postnatal growth thereafter. However, such research is mostly focused on the relatively small sample of children with the poorest growth who may be clinically categorized as “failing to thrive,” whereas the current study involves the normal spectrum of NWG and thus is more representative of the entire population. Problems with children's behavior have been linked to factors such as postterm gestational age and lighter weight at birth.^{30–33} Yang et al⁸ developed trajectories of growth from birth to 5 years in the PROBIT cohort

and showed that faster gains in weight and length, particularly during infancy, were associated with fewer externalizing problems at 6 years.

Despite evidence that faster postnatal weight gain is beneficial, others have found no association with children's neurocognitive development. Belfort et al⁹ reported that postnatal growth, measured as the change in weight z-scores between birth and 6 months, was not associated with language or visuomotor abilities at 3 years ($n = 872$). It is difficult to explain the differences in findings between our study and Belfort et al,⁹ but they may be attributable to nonlinearity of the association between postnatal growth and cognitive outcomes, age at assessment, or lack of power owing to Belfort et al's⁹ smaller sample.

Disparities across studies raise the possibility that the association between NWG and IQ is attributable to unmeasured or residual confounding, which is a limitation of all observational research, including ours. It is not possible to know whether parental education and occupation fully account for the influence of parental IQ, which could contribute to NWG through greater vigilance and awareness. Nevertheless, we included a wide range of potential confounders and attempted to account for differences in NWG that were attributable to the trial intervention. The current study was conducted in a large sample of Belarusian children with access to medical services that are comparable to those in high-income countries. From a clinical perspective, the impact of increasing NWG from the

lowest to the highest quartile on children's IQ scores is only 1.5 points, which is not important for the individual child, but small incremental increases in population-level IQ scores may have measurable effects on human capital.³⁴

Slow feeding and difficulties with sucking and swallowing may result in poorer NWG and slower brain growth, which could explain the association we observed between lower NWG and lower IQ scores. Feeding difficulties might also conceivably lead to neonatal hypoglycemia, another potential mechanism for the observed association, by depriving the brain of glucose.³⁵ Although neonatal hypoglycemia may have long-term effects on children's development, there is no consensus on the blood glucose levels or the duration of hypoglycemia that can cause neurologic impairment.^{35,36} Glucose levels were not obtained in our study. A more likely alternative explanation is that feeding difficulties may be a marker of existing neurologic impairment,^{37,38} that is, the direction of cause and effect might be reversed.

CONCLUSIONS

Many mothers have difficulty establishing breastfeeding in the first weeks of life.¹ Most of the literature in this area has focused on recognizing and correcting problems with breastfeeding. Our findings suggest that NWG is associated with children's IQ scores and highlights the importance of intervening early in the management of infants with feeding difficulties.

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