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The impact of short-term predominate breastfeeding on cognitive outcome at 5 years

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Short title: Predominately Breastfeeding and cognitive outcome

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Aim: Breastfeeding is associated with IQ, school attendance and income. Despite the known benefits of breastfeeding, the rate of exclusive breastfeeding up to 6-months is low globally. We examined the effect of short-term breastfeeding on long-term IQ.

Methods: In this secondary analysis of the prospective Cork BASELINE Birth Cohort Study, children were categorised as predominantly breastfed (n = 288) versus exclusively formula-fed (n = 254) at 2-months of age. Infants (n = 404) receiving mixed-feeding were excluded. Outcome was assessed using the KBIT II at 5-years. Multivariable linear regression was used to adjust for confounding variables.

Results: Following adjustment for confounding variables, children, predominately breastfed at 2-months of age, demonstrated increased overall IQ (2.00 points (95% CI: 0.35 to 3.65) ; p = 0.018)

and non-verbal IQ at 5-years of age (1.88 points (95% CI: 0.22 to 3.54); p = 0.027) compared to those never breastfed. No significant relationship was found with verbal IQ (p = 0.154).

Conclusion: A significant increase in composite and non-verbal IQ at 5-years of age was associated with short-term breastfeeding. This study adds to a growing body of evidence that short-term breastfeeding promotes healthy cognitive development.

Keywords: Breastfeeding, Cognition, IQ

Key notes

- This study investigated the impact of predominate breastfeeding at 2 months of age on IQ at 5 years of age.
- A statistically significant relationship was found between children who were predominately breastfed at 2 months and an increase in composite and non-verbal scores.
- Any additional IQ points on a standardised assessment represents a cognitive advantage, which could have a bearing on a child's future outcome.

Background

Breastfeeding has many health benefits for infants including the prevention of infections such as non-specific gastroenteritis (1), acute otitis media and lower respiratory tract infections (2, 3). The World Health Organization (WHO) and the American Academy of Pediatrics (AAP) recommend that infants should be exclusively breastfed up to 6 months of age and partially breastfed up to 1 year of age (4, 5). The WHO estimates that if all children were breastfed as per the WHO guidelines, over 820,000 deaths among children under the age of 5 years could be prevented every year (4).

Despite the known benefits associated with breastfeeding, the rate of exclusive breastfeeding up to 6 months is low globally, with approximately 40% of 0-6 month-old infants being exclusively breastfed. Ireland is not an exception, as demonstrated in the Cork BASELINE birth cohort study and the Growing up in Ireland study, which both reported very low rates of exclusive breastfeeding beyond the first few months of life (6, 7). The BASELINE study reported an exclusive breastfeeding rate of 0.7% (7/966) (6) at 6 months, while the Growing up in Ireland study reported 5.5% (weighted; 6.4% (710/11,131) unweighted) (7). This variance in exclusive breastfeeding rates may be due to the different criteria used to define exclusive breastfeeding. The BASELINE study also revealed that 37% of infants who were formula fed (157/424) had never received breast milk (8).

A WHO report on infant feeding has shown that breastfeeding has a positive impact on IQ, school attendance and income in adulthood (4). A systematic review and meta-analysis conducted by Horta, Loret de Mola & Victoria concluded that breastfeeding was associated with an increase in results on intelligence tests, even after adjusting for maternal IQ (9). However, there is ongoing debate about the effect of breastfeeding on cognitive development. Some studies have indicated that breastfeeding bolsters cognitive development, leading to increased IQ and language development (3, 5, 7, 10-20). Conversely, other studies reported that breastfeeding had no impact on cognitive development (21, 22), or, concluded that the small effect noted was

not significant after controlling for confounding variables (23). One of the difficulties when comparing studies has been the high rate of mixed feeding, as few studies were able to control for this to examine the true effect of breastfeeding.

We aimed to investigate the impact of predominate breastfeeding, up to 2 months of age on IQ at 5 years using the Kaufman Brief Intelligence Test II (KBIT-II).

Methods

This was a secondary analysis of data from the Cork BASELINE (Babies After Scope: Evaluating the Longitudinal Impact Using Neurological and Nutritional Endpoints) Birth Cohort Study. The Cork BASELINE cohort study consisted of 2183 participants, with the majority recruited from the SCOPE Ireland maternal study at 20 weeks gestation (http://scopestudy.net). An additional 600 infants were recruited after birth, between 2008 and 2011. The methods and participant characteristics of the Cork Baseline Birth Cohort Study have been detailed elsewhere (24). Our secondary data analysis focused on participants born at term who had complete early feeding data and follow up at 5 years. Infants were excluded for the following reasons: incomplete feeding or 5 year outcome data (n = 1202), gestation age <37 weeks (n = 30), congenital abnormality/birth asphyxia (n = 5), or mixed feeding at 2 months (n = 404). Only children who had been predominately breastfed at 2 months (n = 288) and children who had never been breastfed at 2 months (n = 254) were eligible for inclusion in the study.

Neurodevelopmental Assessment

The Kaufman Brief Intelligence Test II (KBIT-II) was administered to all children in the present study at 4.8-5.5 years of age by appropriately trained research staff. The KBIT-II yields three scores: Verbal, Non-verbal, and IQ Composite scores (25). All standard scores have a mean of 100 and standard deviation of 15, with the average range being defined as scores between 85 and 115, and higher scores indicating a greater level of intelligence (25).

Measurement of Breastfeeding at 2 months:

Breastfeeding at 2 months was dichotomized into 'Predominately breastfed at 2 months follow-up' and 'never breastfed'. Children were considered predominately breastfed if their Mother had answered breastfed to the 'method of feeding' question on the 2-month questionnaire in the BASELINE study. Children were considered never breastfed if their mother answered 'Never breastfed' to the question 'Was your baby ever breastfed' on the 2-month questionnaire in the BASELINE study (24).

Statistical Analysis

We explored the impact of exclusive breastfeeding at 2 months on neurocognitive outcomes as measured via the cognitive verbal and non-verbal scores on the KBIT-II. Separate analyses were performed for each dependent variable of interest. Initially, univariable linear regression was used to investigate the relationship between exclusive breastfeeding and neurocognitive outcome scores. To adjust for potential confounding variables, multivariable linear regression was used. Adjustments were made for the following variables in the multivariable linear regression models: age of child at KBIT and sex of child (Model 2); independent variables in Model 2 + admission to Neonatal Intensive Care Unit (NICU) (Model 3); independent variables in Model 3 + gestational age + birthweight (Model 4); independent variables in Model 4 + relationship status of mother (Model 5); independent variables in Model 5 + household income + socioeconomic index + years of schooling of mother + highest level of education of mother (Model 7). Confounding variables were decided on as per a literature search. All information on the variables was taken from the questionnaires given to parents at the 2 month and 5 year BASELINE visits. Household income, socioeconomic index and years of schooling were based on the 2 month questionnaire while highest maternal education was based on the 5 year questionnaire (24).

Prior to performing the multivariable linear regression analyses, multicollinearity among the independent variables was tested using the variance inflation factor (VIF). Children with missing data on the independent variables were excluded from the analysis. To ensure that the results observed were due to predominate breastfeeding in the first 2 months of life, a sensitivity analysis was performed, excluding infants who continued to be predominately breastfed to 6 months of age. Only infants who were predominately breastfed at 2 months but had stopped breastfeeding or were receiving mixed feeding at 2 months were included and compared to infants who were never breastfed. All tests were two-sided and a p-value < 0.05 was considered to be statistically significant. The statistical analysis was performed using Stata (version 13.0, StataCorp LP, College Station, TX, USA).

Results

Of those who were predominately breastfed at 2 months (n=288), the median (IQR) duration of any breastfeeding was 32 weeks (24 to 50) and the range was 10 weeks to 99 weeks. Of those who were predominately breastfed at 2 months, by 6 months 39.2% (n = 113) were still predominately breastfed, 32.3% (n = 93) were formula-fed and 28.5% (n = 82) received mixed feeding. By 12 months (missing data n = 3) only 10.8% (n = 31) were still predominately breastfed, 59.4% (n = 171) were formula-fed, 8.7% (n = 25) were mixed feeding and 20.1% (n = 58) were classified as “other” feeding type.

In total, 525 participants were included in the regression analysis. The participants were divided into 2 groups based on their feeding status at a 2-month follow-up appointment: those

who 'predominately breastfed up to 2 months' (n = 279) and those who 'never breastfed' (n = 246). Demographic and clinical characteristics overall and by feeding group are shown in Table 1.The mean (*SD*) gestational age was 40.2 (1.1) weeks, the overall mean (*SD*) birth weight was 3571g (445) and the admission rate to the Neonatal Intensive Care Unit was 5.3%. The majority of mothers were in a relationship (96.8%) and 61.3% had a university degree or higher qualification (see Table 1). Women with a higher level of education, higher household income and higher socio-economic index were more likely to predominately breast-feed at 2 months. Women in a relationship and those who didn't smoke during pregnancy were also more likely to predominately breast-feed. Female children and children with a higher gestational age were more likely to be predominately breast-fed.

The results of the linear regression analyses (unadjusted and adjusted) are summarised in Table 2. For the KBIT-II composite score, there was a statistically significant relationship between predominate breastfeeding at 2 months and cognitive score at 5 years. On average, children who were predominately breastfed scored 2.47 points higher (95% CI: 1.00 to 3.95, p = 0.001) than children who were never breastfed (Model 1). After adjustment for potential confounding variables (Model 7), the relationship remained statistically significant with children who were predominately breastfed at 2 months scoring 2.00 points higher (95% CI: 0.35 to 3.65, p = 0.018) than children who were never breastfed.

A similar pattern of results was evident in the KBIT-II non-verbal scores (see Table 2). For the KBIT-II non-verbal score, a statistically significant relationship was found between predominately breastfeeding at 2 months and non-verbal score at 5 years. On average, children who were predominately breastfed scored 1.68 points higher (95% CI: 0.22 to 3.15, p = 0.024) than children who were never breastfed (Model 1). After adjustment for potential confounding variables (Model 7), the relationship remained statistically significant with children who were predominately breastfed at 2 months scoring 1.88 points higher (95% CI: 0.22 to 3.54, p = 0.027) than children who were never breastfed.

For the KBIT-II verbal scores, a statistically significant relationship was found between predominately breastfeeding at 2 months and verbal score at 5 years. On average, children who were predominately breastfed scored 2.51 points higher (95% CI: 0.83 to 4.19, p = 0.004) than children who were never breastfed (Model 1). However, after adjustment for potential confounding variables (Model 7), the relationship was no longer significant (p = 0.154).

The linear regression analysis was rerun using a subgroup of our cohort in order to ensure that the effect we were observing was due to predominate breastfeeding in the first 2 months of

life. Infants who continued to be predominately breastfed up to 6 months of age and infants for whom information on feeding at 6 months was unavailable were removed. After removal of those infants and adjusting for potential confounding variables (Model 7), the magnitude of the differences in cognitive outcome scores between the two groups remained similar. For the KBIT-II composite score, children who were predominately breastfed (n=170) scored 2.19 points higher on average (95% CI: 0.27 to 4.11, p = 0.025) than children who were never breastfed (n=242). Similarly, for the KBIT-II non-verbal score, children who were predominately breastfed (n=171) scored 2.14 points higher on average (95% CI: 0.27 to 4.00, p = 0.025) than children who were never breastfed (n=242). A statistically significant difference was not found in KBIT-II verbal scores between the two groups (p=0.280).

Discussion

Our results demonstrate that predominately breastfeeding, even for a short duration in early infancy, has a positive impact on the cognitive development of the child. This adds to the wealth of evidence supporting a positive association between breastfeeding and cognitive development (3, 4, 7, 10, 12, 14-16, 18-20, 26-28). Children who were predominately breastfed at 2 months had a higher KBIT-II composite score at 5 years than children who were never breastfed. Even after adjusting for potential confounding (model 7) variables, the relationship remained statistically significant. A statistically significant relationship between being predominately breastfed at 2 months and KBIT-II *nonverbal score* at 5 years, remained after adjusting for the confounding variables. Breastfeeding predominately at 2 months was not associated with a higher KBIT-II *verbal score* at 5 years.

Previous studies have shown that a longer duration of exclusive breastfeeding is necessary in order to see a benefit in cognitive development from breastfeeding (10, 12, 14). However, our study demonstrates that predominate breastfeeding, even if limited to 2 months of age, results in an increase in cognitive ability at 5 years. This significance was robust following sensitivity analysis, which excluded infants who continued to breastfeed predominately to 6 months. This is noteworthy with respect to duration, with the potential benefits from even a short duration of breastfeeding providing a positive message for mothers to encourage them to provide at least 2 months of predominate breastfeeding (4, 5).

Our data is consistent with the findings of Jedrychowski *et al.* who reported that as little as 3 months of exclusive breastfeeding has a beneficial impact on the cognitive development of infants (12). In this prospective cohort study, infants who were exclusively breastfed for up to 3 months had IQs that were on average 2.1 points higher than IQs in the control group at 7 years of

age. However, there were some marked dissimilarities between our studies. Our control group was ‘never breastfed' but Jedrychowski *et al.* had a control group that received mixed feeding. Our follow-up was conducted at 5 years using KBIT-II whereas Jedrychowski *et al.* followed up their participants at 7 years of age using the Wechsler Intelligence Test for Children (12) . In the Growing Up in Ireland Study, it has been reported that *any* breastfeeding during early infancy was positively associated with an advantage on standardized cognitive assessments. At 9 months of age, in comparison to infants who were never breastfed, those who were breastfed had 1.2 times the odds of achieving age-appropriate developmental milestones on the problem-scoring component of the Ages and Stages Questionnaire. They also had 1.3 and 1.6 times the odds of meeting age-appropriate cut-offs for fine and gross motor skills respectively (7).

Bernard *et al.* noted that any duration of breastfeeding was associated with a positive effect on cognition (27), while Cai *et al.* reported that breastfeeding had a positive impact on the development of memory and language (16). These effects are not short lived and result in improved educational attainments including higher school test scores and higher teacher ratings of reading and mathematics (19), as well as improved intelligence and higher income levels in adulthood (11, 15). Evenhouse and colleagues used sibling comparisons to decrease sample selection bias and demonstrated a causal relationship between breastfeeding and cognitive development (20). Studies including preterm infants have suggested that preterms derive more benefits from breastmilk than full-term infants (26) and that they have a substantial developmental advantage compared to preterm infants that were fed formula (18).

Imaging studies have demonstrated that breastfed children have a larger brain as well as larger volumes of total gray matter, total cortical gray matter and subcortical gray matter compared to infants who were bottle-fed (28). These children also scored higher on the Kaufman Brief Intelligence Test and the Wechsler Abbreviated Scale of Intelligence (28). Deoni and colleagues compared white matter microstructures, using MRI scans, in healthy children from the age of 10 months to 4 years. They demonstrated that early exclusive breastfeeding, to at least 3 months, was associated with an increase in development of white matter regions such as the frontal and temporal white matter, peripheral aspects of the internal capsule and corticospinal tracts, superior longitudinal fasciculus, and superior occipital frontal fasciculus. Exclusively breastfed infants had improved scores on the Mullen Scales of Early Learning in the areas of executive function, planning, social-emotional function, and language. These areas are commonly associated with the brain regions mentioned above (29). A study that investigated the development of electrical brain activity (EEG) in infants noted a difference between breastfed and non-breastfed infants. Between 3 and 6 months, the spectral power increased across the

frequency bands for all groups; however, the increase in the 0.1-9 Hz EEG band was greater in formula-fed infants than in breastfed infants and reached a peak 3 months prior to that of breastfed babies. The significance of these differences and how they map onto changes in developmental progression are unclear (13).

Various mechanisms have been proposed to explain the effect of breastfeeding on cognition. It has been hypothesized that docosahexaenoic (DHA) and arachidonic (AA) acids in breastmilk are responsible for the increase in cognitive ability. These are major lipid components of breast milk and are important for cortical brain development, as well as retinal development (12, 13, 28, 30). Others have suggested that it is the act of breastfeeding itself; the bond created between mother and child, the skin-to-skin contact and the overall increased sensory stimulation that promotes cognitive development (12, 21).

Although many papers have shown improved cognitive development in breastfed infants, the strength of that improvement and the exact causative role of breastmilk is unclear. Many have argued that there is no convincing evidence for a causal relationship between breastfeeding and cognitive development (17) and others have concluded that this association can be explained by maternal intelligence (21) and sociodemographic factors (22, 23).

There are limitations in the reported literature. The definition of breastfeeding varies between studies, with some defining predominate breastfeeding as exclusive breastfeeding. The duration of breastfeeding and the extent of exclusive breastfeeding varies greatly from study to study. This could account for the conflicting results. In our study, we compared 2 clearly defined groups; one which was exclusively breastfed for at least 2 months and the second who never had a single breastfeed. For example, in one study the non-breastfeeding group was defined as breastfeeding for less than 6 months (17). Many studies have relied on recall from mothers on breastfeeding duration and this may have resulted in measurement error (15, 27), whereas mothers in our study supplied this information throughout the Cork BASELINE study. Another limitation is that in most studies maternal intelligence is not available (7, 27).

One of the limitations in our study is that we could not adjust our results for maternal IQ as we did not measure it directly. A systematic review and meta-analysis conducted by Horta, Loret de Mola and Victoria showed that infants who had been breastfed had an increase of 3.44 IQ points which was reduced to 2.62 points after controlling for maternal IQ. Therefore, if maternal IQ was to be adjusted for the effect measure may be lower than 2 IQ points. That said, years of schooling and highest education level of the mother were considered as potential confounding factors. Many studies have demonstrated that adjusting for maternal IQ results in a non-

statistically significant relationship between breastfeeding and cognitive ability (3, 10, 14); and there is little doubt that it is an important confounding variable to include in future studies. Another significant limitation is that the actual duration of predominate breastfeeding was not taken into account. Mothers continued to predominately breastfeed for longer than 2 months increasing the effect of the exposure. However, when we removed those infants who continued to receive predominate breastfeeding to 6 months, the effect seen did not change significantly.

A final limitation of this study is that we did not capture any information on the frequency of feeding or any information on the home environment. Some believe that it is not breastmilk that provides the benefits to cognition but rather the stimulation the infant receives during breastfeeding or the stimulation that may occur in the infant's home environment (22, 23). Zhou et al. reported that the quality of the home environment, as measured by the Home Screening Questionnaire, was the strongest predictor of IQ (22). Hence, future studies should attempt to capture information on the infant's home environment as well as the frequency of both breastfeeding and bottle-feeding.

In conclusion, we have shown that a large cohort of infants predominately breastfed for the first 2 months of life had a higher IQ score than a similar cohort of infants who were exclusively formula-fed. While the clinical relevance of an additional 2 IQ points on a standardised assessment is unknown, any additional IQ points represent a cognitive advantage which could have a bearing on a child's future outcome. This study offers additional evidence to support the hypothesis that predominate breastfeeding, even for a short period, promotes cognitive development. Whilst not all mothers can breastfeed for extended periods, all should be encouraged by our findings.

Abbreviations

American Academy of Pediatrics (AAP)

Arachidonic (AA)

Docosahexaenoic (DHA)

Kaufman Brief Intelligence Test II (KBIT-II)

Variance inflation factor (VIF)

World Health Organization (WHO)

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Conflict of interest

None to declare.

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Tables

Table 1. Demographic and clinical characteristics of participants overall and by feeding group

	Overall (n = 525)		Exclusively breastfed at 2 months (n = 279)		Never breastfed (n = 246)		
	mean	(SD)	mean	(SD)	mean	(SD)	*p*-value[1]
Age (years) of child at test	5.1	(0.1)	5.1	(0.1)	5.1	(0.1)	0.940
Gestational age (weeks)	40.2	(1.1)	40.3	(1.0)	40.1	(1.1)	0.044
Birthweight (g)	3571	(445)	3605	(450)	3533	(437)	0.065
Socioeconomic index	43.7	(15.8)	48.1	(16.4)	38.8	(13.6)	<0.001
Years of schooling of mother	13.4	(0.8)	13.4	(0.8)	13.4	(0.7)	0.634
	n	(%)	n	(%)	n	(%)	*p*-value[2]
Sex: Male	273	(52.0)	129	(46.2)	144	(58.5)	0.005
Admitted to NICU	28	(5.3)	12	(4.3)	16	(6.5)	0.262
Mother in a relationship	508	(96.8)	277	(99.3)	231	(93.9)	0.001
Mother smoked during pregnancy	31	(5.9)	5	(1.8)	26	(10.6)	<0.001
Household income							<0.001
<21K	27	(5.1)	6	(2.2)	21	(8.5)	
21-42K	96	(18.3)	39	(14.0)	57	(23.2)	
43-63K	118	(22.5)	54	(19.4)	64	(26.0)	

64-84K	132	(25.1)	81	(29.0)	51	(20.7)
85-105K	74	(14.1)	42	(15.1)	32	(13.0)
106-140K	69	(13.1)	50	(17.9)	19	(7.7)
>140K	9	(1.7)	7	(2.5)	2	(0.8)
Highest education level of mother						<0.001
Secondary level or lower	41	(7.8)	3	(1.1)	38	(15.4)
Certificate/Diploma	162	(30.9)	52	(18.6)	110	(44.7)
Degree	135	(25.7)	83	(29.7)	52	(21.1)
Higher/graduate diploma	88	(16.8)	64	(22.9)	24	(9.8)
Masters/PhD	99	(18.9)	77	(27.6)	22	(8.9)

[1]from independent samples t-test;

[2]from chi-squared test

Table 2. Results of linear regression analyses investigating the relationship between exclusive breast-feeding and neurodevelopmental outcome at 5 years

	KBIT-II composite (n=524)		KBIT-II verbal (n=524)		KBIT-II non-verbal (n=525)	
	regression coefficient (95% CI)	p-value	regression coefficient (95% CI)	p-value	regression coefficient (95% CI)	p-value
Model 1: unadjusted (exclusive breast-feeding at 2 months vs never breast-fed)	2.47 (1.00 to 3.95)	0.001	2.51 (0.83 to 4.19)	0.004	1.68 (0.22 to 3.15)	0.024
Model 2: Model 1 + adjusted for age of child at test and sex	2.19 (0.72 to 3.67)	0.004	2.17 (0.49 to 3.85)	0.011	1.58 (0.10 to 3.05)	0.036
Model 3: Model 2 + adjusted for admission to NICU	2.17 (0.69 to 3.65)	0.004	2.11 (0.43 to 3.79)	0.014	1.58 (0.11 to 3.06)	0.036
Model 4: Model 3 + adjusted for gestational age and birthweight	2.14 (0.66 to 3.62)	0.005	2.09 (0.40 to 3.78)	0.015	1.55 (0.07 to 3.04)	0.040
Model 5: Model 4 + adjusted for relationship status of mother	1.96 (0.47 to 3.45)	0.010	1.94 (0.23 to 3.65)	0.026	1.41 (-0.09 to 2.91)	0.065
Model 6: Model 5 + adjusted for household income, socioeconomic index, years of schooling of mother and highest education level of mother	1.95 (0.30 to 3.59)	0.021	1.41 (-0.47 to 3.28)	0.141	1.71 (0.05 to 3.38)	0.044
Model 7: Model 6 + adjusted for smoking during pregnancy	2.00 (0.35 to 3.65)	0.018	1.37 (-0.51 to 3.24)	0.154	1.88 (0.22 to 3.54)	0.027