

REVIEW ARTICLE

Breastfeeding and intelligence: a systematic review and meta-analysis

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ABSTRACT

Aim: This study was aimed at systematically reviewing evidence of the association between breastfeeding and performance in intelligence tests.

Methods: Two independent searches were carried out using Medline, LILACS, SCIELO and Web of Science. Studies restricted to infants and those where estimates were not adjusted for stimulation or interaction at home were excluded. Fixed- and random-effects models were used to pool the effect estimates, and a random-effects regression was used to assess potential sources of heterogeneity.

Results: We included 17 studies with 18 estimates of the relationship between breastfeeding and performance in intelligence tests. In a random-effects model, breastfed subjects achieved a higher IQ [mean difference: 3.44 points (95% confidence interval: 2.30; 4.58)]. We found no evidence of publication bias. Studies that controlled for maternal IQ showed a smaller benefit from breastfeeding [mean difference 2.62 points (95% confidence interval: 1.25; 3.98)]. In the meta-regression, none of the study characteristics explained the heterogeneity among the studies.

Conclusion: Breastfeeding is related to improved performance in intelligence tests. A positive effect of breastfeeding on cognition was also observed in a randomised trial. This suggests that the association is causal.

INTRODUCTION

Breastfeeding has clear short-term benefits for child health, reducing mortality and morbidity from infectious diseases (1). Furthermore, infants who are exclusively breastfed in early life present lower morbidity from gastrointestinal and allergic diseases, whilst showing similar growth rates to nonbreastfed children (2). With respect to the long-term consequences of breastfeeding, evidence, mainly from high-income countries, suggests that duration of breastfeeding is positively associated with performance in intelligence tests. A meta-analysis that included 14 observational studies reported that breastfeeding was associated with a 3.5 point (95% confidence interval: 1.9; 5.0) higher score in intelligence tests (3). This positive effect of breastfeeding has also been observed in a randomised trial. In Belarus, intelligence quotients (IQ) at 6.5 years of age were on average 7.5 points higher among those children who were allocated to breastfeeding promotion groups (4). Furthermore, in the United Kingdom, preterm children whose mother chose to provide breast milk presented a higher IQ than those who were formula-fed. Furthermore, those children whose mothers tried to provide breast milk but failed to do so had an IQ similar to that observed among those children whose mothers did not try to provide breast milk (5).

It has also been observed that this IQ gain has a long-term impact and subjects who have been breastfed have improved performance in school tests (6) and higher education in adolescence and adulthood (7,8). This beneficial effect of breastfeeding could be due to the presence of long-chain polyunsaturated fatty acids, such as arachidonic acid and docosahexaenoic acid in breast milk (9). Breastfed infants have higher concentrations of these fatty acids that are positively associated with brain development (10,11). On the other hand, studies that used the FADS2 gene as proxy for docosahexaenoic acid exposure have reported controversial findings (12–14).

In the 2013 review, maternal IQ was an important confounder that accounted for part of the association between breastfeeding and performance in intelligence tests (3). By updating the systematic review and increasing the number of studies, we expected to obtain more precise estimates from studies that controlled for maternal IQ.

Abbreviations

IQ, Intelligence quotient.

Key Notes

- Breastfeeding is associated with improved performance in intelligence tests.
- The association persists after adjustment for maternal IQ.
- Long-term follow-up studies suggest that breastfeeding impacts on schooling and adult income.

We carried out a systematic review and meta-analysis of the evidence for a relationship between breastfeeding and performance in intelligence tests.

METHODS

We updated systematic reviews on the association between breastfeeding and performance in intelligence tests published in 2007 (15) and 2013 (16). First, two independent reviewers (B.L.H. and C.L.M.) carried out parallel literature searches, using the same search strategy. Any disagreement was solved by consensus (17). Medline, LILACS, SCIELO and Web of Science databases were searched for observational and randomised studies that evaluated the association between breastfeeding and performance in intelligence tests. As the previous update of the systematic review covered manuscripts that had been published before September 2011 (16), we searched for papers that had been published from September 2011 to December 2014.

The literature search used the following terms: breastfeeding; breast feeding; breastfed; breastfeed; bottle feeding; bottle fed; bottle feed; infant feeding; human milk; formula milk; formula feed; formula fed; and weaning. The breastfeeding terms were combined with the following keywords for performance in intelligence tests: schooling; development; and intelligence.

After excluding duplicates, titles and abstracts were perused to exclude those that were obviously irrelevant. The full texts of the remaining studies were retrieved, and relevant articles were identified. In addition to the electronic search, reference lists of the articles identified were searched, and we perused the Web of Science Citation Index for manuscripts citing the identified articles. Attempts were made to contact the authors of all studies that did not provide sufficient data to estimate the pooled effect.

In the literature search, we employed the following selection criteria to include studies in review:

- the study should have an internal comparison group;
- cognition had to be measured using standard tests;
- study should have been carried out among subjects older than 1 year of age;
- estimates had to be adjusted for stimulation or interaction with the child.

The type of comparison group (never breastfed, breastfed for less than x months, etc.) and exposed group (ever breastfed, breastfed for more than x months, exclusively breastfed for x months) was not considered as eligibility criteria.

Using a standardised protocol, two reviewers extracted the following information from each study:

- sample size
- follow-up rate: proportion of subjects lost during the study;
- study design

- length of recall of breastfeeding duration: elapsed time between weaning and collect of the information on breastfeeding duration;
- type of comparison group (e.g. never breastfed, breastfed for less than a given number of months);
- source of breastfeeding information;
- control for confounding: the estimates were adjusted for maternal IQ;
- year of birth of subjects;
- age at outcome assessment: age at which performance in intelligence tests was evaluated.

Disagreements were resolved by consensus.

Effect measures were reported as weighted mean differences in performance in intelligence tests and their 95% confidence interval, and subjects were classified as either breastfed or nonbreastfed, according to the definition used in each study. A positive mean difference denoted a higher score among breastfed subjects. Pooled effects were calculated using both fixed- and random-effects models. Heterogeneity among studies was assessed using the Q-test and I-square; if either test suggested that the between-study variability was higher than expected, the random-effects model was used (18). Funnel plot and Egger test were used to investigate publication bias (19). All analyses were also stratified by study size to assess the impact of publication bias on the pooled estimate.

Meta-regression was used to evaluate the contribution of study characteristics to the between-study variability (20). Study characteristics were included as covariates in the meta-regression individually, rather than using an overall score of study quality. This approach allowed the identification of aspects of study design that were responsible for heterogeneity between studies.

RESULTS

After excluding duplicates, 6621 abstract were screened, 36 full-text articles were assessed for eligibility, and four studies were identified in the update of the systematic review (Fig. 1). The list of the references excluded after being reviewed is shown in Table S1. The meta-analysis included 17 studies with 18 estimates on the relationship between breastfeeding and performance in intelligence tests. Table 1 shows that all studies indicated a beneficial effect of breastfeeding on performance in intelligence tests, but the confidence interval included the reference (0) in five studies. As there was clear heterogeneity among studies, the estimates were pooled using a random-effects model. The pooled effect estimate shows that breastfed subjects achieved a higher performance in intelligence tests [mean difference: 3.44 points (95% confidence interval: 2.30; 4.58)].

Table 2 shows that the positive effect of breastfeeding on cognition is not likely due to a publication bias because the mean effect was similar among studies with sample sizes <500 and ≥500 subjects. Table 2 also shows that studies that controlled for maternal IQ reported a

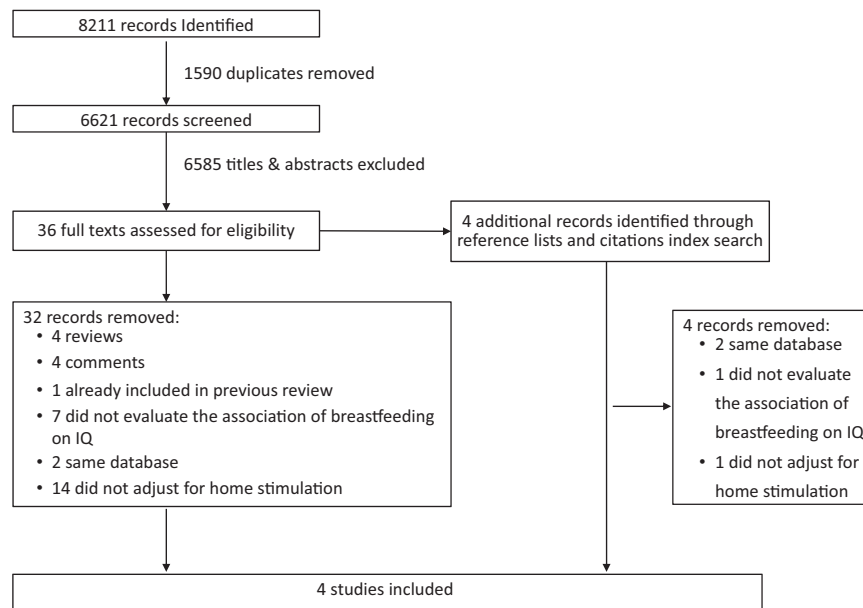


Figure 1 Flow diagram of study selection.

smaller benefit of breastfeeding [mean difference 2.62 points (95% confidence interval: 1.25; 3.98)]. Studies that evaluated subjects aged between 10 and 19 years also reported a smaller benefit from breastfeeding [mean difference: 1.92 points (95% confidence interval: 0.43; 3.40)] than studies involving younger subjects [mean difference: 4.12 points (95% confidence interval: 2.50; 5.73)]. In the meta-regression, none of the variables related to study characteristics explained the heterogeneity among the studies.

DISCUSSION

In this meta-analysis, we observed that breastfeeding is positively associated with performance in intelligence tests in childhood and adolescence; subjects who had been breastfed had an average gain of 3.44 points. It has been suggested that maternal IQ could be an important residual confounder in this association (21), but we demonstrated that the association was still present among studies that controlled for maternal IQ [pooled odds ratio: 2.62 (95% confidence interval: 1.25; 3.98)].

As breastfeeding mothers are more likely to provide a cognitively stimulating environment for their infants (21), it has been suggested that breastfeeding could be a marker of parenting practices that promote child development (22), such that the positive effect of breastfeeding on cognition could be due to the family environment and not to nutrition. In this meta-analysis, we excluded those studies that did not adjust their estimates for variables measuring home stimulation, reducing the likelihood that the association was due to differences in the home environment. Residual confounding by socio-economic status is another

methodological issue that should be taken into consideration. In high-income countries, income is positively associated with breastfeeding duration (23), and performance in intelligence tests is positively related to socio-economic position (24,25).

Only two studies reported associations with exclusive breastfeeding duration. Wigg et al. (26) observed that IQ at 12 years of age was slightly higher among those subjects who had been exclusively breastfed in the first 6 months, in relation to those who were never breastfed, but the confidence interval included the reference [0.8 points (95% confidence interval: -1.9; 3.5)]. Eickman et al. (27) observed that children who had been exclusively breastfed in the first month had significantly better performance in intelligence tests than those who were partial (also receiving formula) or not breastfed at 1 month [difference 3 points (95% confidence interval: 0.48; 5.53)].

Randomised studies are not susceptible to self-selection bias or residual confounding if properly designed and conducted. In a cluster randomised trial in Belarus, Kramer et al. (4) allocated 31 maternity hospitals and affiliated clinics to either receive or not receive the baby-friendly hospital initiative. Duration of total and exclusive breastfeeding was higher in the intervention group, as well as the performance in intelligence tests at 6.5 years, with a cluster mean IQ difference of 7.5 points (95% confidence interval: 0.8; 14.3). This result reinforces the evidence of observational studies that breastfeeding may have a long-term consequence on cognition.

In order to assess the impact of the main threat to the validity of epidemiologic studies, we estimated the pooled effect among those studies that were less prone to

Table 1 Breastfeeding and cognitive development in later life: studies included in ascending order of publication

Author, Year	Study design	Mean age at assessment	Cognitive Development Assessment	Gender	Categorisation of breastfeeding	Mean difference Intelligence test (Standard error)
Morrow-Tlucak, 1988 (30)	Cohort	2 years	Bayley Scales of Infant Development – MDI	All	Breastfed ≥ 4 months vs. never breastfed	9.1 (3.68)
Lucas, 1992 (5)	Cohort	8 years	WISC-R	All	Ever breastfed vs. never breastfed	7.6 (1.84)
Johnson, 1996 (31)	Cohort	3 years	PPVT-R	All	Ever breastfed vs. never breastfed	5.0 (2.35)
Wigg, 1998 (26)	Cohort	12 years	Wechsler Full Scale	All	Exclusive or predominant breastfed at 6 months vs. never breastfed	0.8 (1.38)
Jacobson, 1999 (32)	Cohort	11 years	WISC-R	All	Ever breastfed vs. never breastfed	4.0 (1.49)
Quin, 2001 (33)	Cohort	5 years	PPVT-R	Male	Breastfed ≥ 6 months vs. never breastfed	5.8 (0.87)
Quin, 2001 (33)	Cohort	5 years	PPVT-R	Female	Breastfed ≥ 6 months vs. never breastfed	8.2 (0.87)
Evenhouse, 2005 (34)	Cross-sectional	15 years	PPVT	All	Ever breastfed vs. never breastfed	1.68 (0.94)
Clark, 2006 (35)	Cohort	5 years	Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R)	All	Breastfed > 8 months vs. breastfed for < 2 months	1.0 (1.09)
Der, 2006 (21)	Cohort	3 years	Peabody individual achievement test	All	Ever breastfed vs. never breastfed	0.52 (0.36)
Gibson-Davis, 2006 (36)	Cohort	3 years	Peabody Picture Vocabulary Test – Third Edition	All	Breastfed ≥ 1 months vs. never breastfed	1.72 (0.60)
Eickman, 2007 (27)	Cohort	1 year	Bayley Scales of Infant Development II	All	Exclusive breastfed for ≥ 1 months vs. partial/none < 1 month	3.0 (1.29)
Zhou, 2007 (37)	Cohort	4 year	Stanford-Binet Intelligence Scale	All	Breastfed > 6 months vs. never breastfed	0.80 (1.29)
Whitehouse, 2011 (38)	Cohort	10 years	PPVT-R	All	Predominant breastfed at 6 months vs. never breastfed	4.04 (1.31)
Smither, 2012 (39)	Cohort	8 years	Wechsler Intelligence Scale for Children (WISC) Version III	All	Breastfed for ≥ 6 months vs. breastfed for < 6 months	0.97 (0.24)
Belfort, 2013 (40)	Cohort	7 years	KBIT-II verbal	All	Breast milk only at 6 months vs. never breastfed	5.59 (1.49)
Bernard, 2013 (41)	Cohort	3 years	ASQ	All	Ever breastfed vs. never breastfed	6.2 (1.89)
Huang, 2014 (42)	Cohort	6 years	Passage Comprehension Test – Woodcock-Johnson Revised	All	Ever breastfed vs. never breastfed	3.46 (0.98)

residual confounding, publication bias and misclassification. We identified 4 studies that had a large sample size (≥ 500 participants), controlled for confounding by maternal IQ and whose recall time on breastfeeding duration

was < 3 years. According to these high-quality studies, breastfeeding improved the performance in intelligence tests [mean difference 1.76 points (95% confidence interval: 0.25; 3.26)].

Table 2 Breastfeeding and mean difference in cognitive development scores in later life: random-effects meta-analyses by subgroup

	Number of estimates	Mean difference (95% confidence interval)	p-value	% heterogeneity explained
Age group				
1 to 9 years	13	4.12 (2.50; 5.73)	<0.001	6.4%
10 to 19 years	5	1.92 (0.43; 3.40)	0.02	
Study size				
<500 participants	7	3.61 (1.59; 5.63)	<0.001	0.0
≥500 participants	11	3.36 (1.97; 4.74)	<0.001	
Control for maternal IQ				
No	9	4.10 (1.94; 6.25)	<0.001	3.9%
Yes	9	2.62 (1.25; 3.98)	<0.001	
Setting				
High-income country	16	3.65 (2.40; 4.90)	<0.001	0.0
Middle-/low-income country	2	1.88 (−0.07; 3.83)	0.06	
Categorisation of breastfeeding				
Ever breastfed	7	3.62 (1.66; 5.59)	<0.001	0.0
Breastfed for a given number of months	11	3.40 (1.73; 5.07)	<0.001	
Total	18	3.44 (2.30; 4.58)		

It has been reported that subjects who were breastfed have higher educational attainment (7,8). Victora et al. (28) reported that breastfeeding was positively associated with IQ, higher education and income in adulthood among subjects who have been followed since birth in a southern Brazilian city. Income among those subjects who had been breastfed for at least 12 months was 20% higher than the average, and IQ explained 72% of the effect of breastfeeding on income. This study also reported a significant dose–response association with the duration of exclusive or predominant breastfeeding; separate analyses of exclusive breastfeeding duration were not possible because of the small number of infants who were only fed with breast milk.

This meta-analysis suggests that breastfeeding is associated with improved performance in intelligence tests in childhood and adolescence. The long-term impact of this increased performance in intelligence tests is an issue open to debate. But as mentioned above, recently published studies reported that breastfed subjects also have a higher income in adulthood.

With respect to the mechanisms that would explain this association, this could be due to the presence of long-chain polyunsaturated fatty acids, such as arachidonic acid and docosahexaenoic acid, in breast milk (9). In addition to these properties of breast milk, breastfeeding helps mothers

to bond with their child (29) and thus contributes to child development. But the finding of Lucas et al. (5) that preterm babies who received breast milk have a higher IQ suggests that the nutritional properties of breast milk seem to have an effect.

CONCLUSION

This meta-analysis shows that breastfeeding is related to improved performance in intelligence tests (3.44 points). Maternal IQ is an important confounder, but breastfeeding was associated with a gain in performance in IQ tests even among studies that controlled for maternal intelligence. A positive effect of breastfeeding on cognition was also observed in a randomised trial. This suggests that this association is causal.

CONFLICT OF INTEREST AND FUNDING STATEMENT

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. List of full text articles excluded from final meta-analysis.