Breastfeeding and neurodevelopmental outcomes

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Purpose of review
Breastfeeding has clear short-term benefits for child survival. Concerning its long-term consequences, it has been reported that subjects who had been breastfed would have a better performance in intelligence tests. In this review, we perused the recently published studies on the association of breastfeeding with developmental outcomes.

Recent findings
A meta-analysis published in 2015 reported that intelligence quotient (IQ) was 3.44 points (95% confidence interval: 2.30; 4.58) higher among subjects who had been breastfed, and this association was observed even among those studies that controlled for maternal IQ. In the present review, we identified two studies that reported that duration of breastfeeding was positively associated with IQ in childhood, whereas another study reported that cognitive score at 67.9 years of age was higher among those subjects who had been breastfed for at least 6 months. Furthermore, two studies reported that the small gain in IQ was associated with higher school achievement and income in adulthood. Concerning the possible mechanisms for the effect of breastfeeding on development, children who had been breastfed showed greater gray matter volume in the left and right parietal and left temporal lobes and more activation in the right frontal and temporal lobes for perception tasks, whereas for the language task, the activation was higher in the left temporal lobe. Moreover, it has been reported that subcortical gray matter volume mediated the association between breastfeeding and IQ.

Summary
The new studies identified in the review reinforce the evidence that breastfeeding has long-term consequences on performance in intelligence tests. In addition, this association between breastfeeding and development has long-term consequences on human capital, increasing earning ability.

Keywords
breastfeeding, development, human capital, intelligence

INTRODUCTION

Breastfeeding has clear short-term benefits, reducing mortality and morbidity from infectious diseases [1]. Concerning the long-term consequences, a meta-analysis including 17 studies reported a higher intelligence quotient (IQ) among subjects who had been breastfed [mean difference: 3.44 points (95% confidence interval (CI): 2.30; 4.58)]. In addition, an association of breastfeeding with IQ was observed, even among those studies that controlled for maternal IQ [mean difference: 2.62 points (95% CI: 1.23; 3.98)] [2]. Moreover, breastfeeding would also protect against obesity, and a meta-analysis reported that even among high-quality studies, those subjects who had been breastfed were less likely of being considered as overweight/obese [pooled odds ratio: 0.87 (95% CI: 0.76; 0.99)]. The present review was aimed at updating the available evidence of the association of breastfeeding with developmental outcomes.

METHODOLOGICAL ISSUES

Most of the studies on the long-term consequences of breastfeeding have been carried out in high-income countries, in these settings breastfeeding duration is higher among children from families with high socioeconomic status [3]. As socioeconomic status is also positively associated with performance in intelligence tests, positive confounding would overestimate the benefits of breastfeeding on performance in intelligence tests. Therefore, in the interpretation of the findings of these studies, the

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KEY POINTS

- Breastfeeding is associated with improved performance in intelligence tests.
- Breastfeeding also has long-term economic consequences, increasing earning ability.
- Increase in breastfeeding rates will have an economic impact at the community level.

possibility that the observed association was due to residual confounding by socioeconomic status must be taken into consideration.

The positive association between breastfeeding and performance in intelligence tests could also be due to self-selection bias. It has been reported that breastfeeding mothers are more likely to be health-conscious and to stimulate their children at home [4]. In addition, home stimulation is positively associated with child development. Indeed, Yousafzai *et al.* [5] observed that children who had been randomly allocated to receive a responsive stimulation intervention had improved cognition, language and motor skills at 4 years of age. Similar findings have been reported by other studies [6]. The self-selection bias could be prevented by measuring home stimulation, which would be a proxy of self-selection. Thereafter, the bias would be treated as a confounder, and the estimates would be adjusted for home stimulation.

To prevent confounding by socioeconomic status and self-selection bias, in this update of the systematic review on the association between breastfeeding and performance in intelligence tests, we excluded those studies that failed to adjust the estimates for socioeconomic variables and stimulation at home.

NEW STUDIES REPORTING ON THE ASSOCIATION BETWEEN BREASTFEEDING AND PERFORMANCE IN INTELLIGENCE TESTS

In 2015, Horta *et al.* [2] published a systematic review and meta-analysis that reviewed the evidence on the association between breastfeeding and performance in intelligence tests, and the main results of this study have already been reported in the introduction. In the present review, we updated the 2015 systematic review. Those studies whose studied population had already been included in the previous review and did not provide new data on the association between breastfeeding and performance in intelligence tests were excluded from the review. We also excluded those studies that failed to adjust the estimates for socioeconomic variables and home stimulation. We identified three studies [7▪▪,8,9] that presented new evidence on the association between breastfeeding and performance in intelligence tests and fulfilled the inclusion criteria (Table 1). Two studies [7▪▪,8] had already been included in the previous review, but provided estimates on the association of breastfeeding with intelligence at older age than in the previous publications. Bernard *et al.* [7▪▪] reported that duration of breastfeeding was positively associated with

Table 1. Prospective studies published since 2015 on the association between breastfeeding duration and performance in intelligence tests

Reference	Study	Country	*N*	Age at assessment	Scale used to assess intelligence	Results/observations
Bernard *et al.* [7▪▪]	EDEN	France	1129	5–6 years	WPPSI-III	Duration of breastfeeding (each month) was positively associated with full-scale [0.20 (95% confidence interval: 0.00; 0.41)] and verbal IQ [0.31 (95% confidence interval: 0.09; 0.52)]
Boucher *et al.* [8]	INMA	Spain	1346	5 years	MSCA	Each month of total [0.19 (95% confidence interval: 0.06; 0.33)], predominant [0.37 (95% confidence interval: 0.05; 0.70)] and exclusive breastfeeding [0.48 (95% confidence interval: 0.04; 0.92)] were associated with performance in IQ test
Rantalainen *et al.* [9]	HBCS	Finland	931	67.9 years	Finnish Defence Forces Basic Intellectual Ability Test	Subjects who had been breastfed had higher total cognitive ability scores. Furthermore, those who had been breastfed for 6 months or more did not show a decrease in verbal subtests score between 20 and 67.9 years

IQ, intelligence quotient; MSCA, McCarthy Scales of Children Abilities; WPPSI-III, Wechsler Preschool and Primary Scale of Intelligence.

full-scale and verbal IQ at 5–6 years of age. Each month of breastfeeding increased full-scale IQ by 0.20 points (95% CI: 0.00; 0.41) and verbal IQ by 0.31 points (95% CI: 0.09; 0.52). Similarly, Boucher *et al.* [8] observed that IQ at 5 years of age was 3.65 points (95% CI: 3.18; 4.12) higher among those children who breastfed for more than 12 months in relation to those who breastfed for 2 or less months. Duration of predominant and exclusive breastfeeding was positively associated with performance in intelligence tests. Rantalainen *et al.* [9] also reported that total cognitive ability score of male subjects who were evaluated at a mean age of 67.9 years was higher among those who had been breastfed for at least 6 months. Furthermore, a decrease in verbal subtest score was observed among those subjects who never breastfed or breastfed for less than 6 months, whereas no decrease was observed among those who breastfed for 6 months or more.

These studies have been carried out in developed countries, but those studied that did not adjust the estimates for confounding for socioeconomic and demographic variables, and home environment were excluded from our review. Therefore, it is unlikely that the observed associations were due to residual confounding and self-selection bias.

The new evidences that we presented above are in agreement with the previous meta-analysis, which reported that IQ was 3.44 points (95% CI: 2.30; 4.58) higher among those subjects who had been breastfed, and an association was observed even after controlling for maternal IQ [mean difference: 2.62 points (95% CI: 1.23; 3.98)] [2]. Boucher *et al.* [8] also adjusted for maternal IQ and its estimate on the effect of breastfeeding was higher than the pooled estimate for studies controlling for maternal IQ. This finding could be due to the fact that the association between duration of breastfeeding and performance in intelligence tests tends to be linear [10], and this study reported on the comparison of extreme categories of duration of breastfeeding. On the other hand, in the 2015 review, six of the 18 estimates included in the meta-analysis, compared subjects who had never vs. ever breastfed. Therefore, the studies identified in the present review reinforce the evidence that breastfeeding has long-term consequences on performance in intelligence tests.

WHAT ARE THE POSSIBLE MECHANISMS UNDERLYING THE ASSOCIATION OF BREASTFEEDING WITH INTELLIGENCE

It has been suggested that the long-chain polyunsaturated fatty acids present in breast milk, which are important for brain development, would be a possible mechanism for the association between breastfeeding and performance in intelligence tests. Bernard *et al.* [7▪▪] observed among children aged 5–6 years from the EDEN cohort that full-scale IQ was higher among those children who had been breastfed and the colostrum presented high levels of arachidonic acid and 3-long-chain polyunsaturated fat acid (3-LC PUFA), whereas children whose colostrum had low levels of arachidonic acid and 3-LC PUFA showed intermediate IQ levels, and those who never breastfed presented the lowest mean IQ.

Moreover, Belfort *et al.* [11▪] observed that the number of days on which preterm infants born less than 30 weeks of gestation received more than 50% of enteral intake as breast milk was associated with larger deep nuclear gray matter and hippocampus volume at term equivalent age. These areas are central for neural function. For example, hippocampal volume is associated with better working memory. Similarly, Ou *et al.* [12▪] noticed that gray matter volume in the left and right parietal lobes and left temporal lobe were greater among children who had been breastfed. Moreover, breastfed children showed higher activation in the right frontal and temporal lobes for perception tasks, whereas for language task, the activation was higher in the left temporal lobe. As brain activation is positively correlated with task performance, these findings reinforce the evidence that breastfeeding is associated with performance in intelligence tests. Indeed, Luby *et al.* [13▪▪] noticed that subcortical gray matter volume significantly mediated the association between breastfeeding and IQ. Therefore, breast milk would foster brain development, and this would be one of the mechanisms for the positive effect of breastfeeding on intelligence.

Bonding between the mother and child is positively associated with neurodevelopmental outcomes, and it tends to be higher among breastfeeding mothers [14]. For this reason, it has been suggested that bonding is another possible mechanism for the positive association of breastfeeding with development. In our review, we identified one study that evaluated the association of breastfeeding with maternal sensitivity and infant temperament at 18 months of age. Mothers who were breastfeeding at 3 months presented higher sensitivity in the interactions with the infant at 6 months, and maternal sensitivity was inversely associated with negative affectivity and infant temperament at 18 months. Mediation analysis showed that maternal sensitivity captured most of the association of breastfeeding with negative affectivity at 18 months [15].

ECONOMIC IMPACTS OF COGNITIVE DEVELOPMENT ASSOCIATED WITH BREASTFEEDING

As previously discussed, the evidence suggest that breastfeeding is associated with an improved performance in intelligence tests, and it has also been reported that breastfeeding is positively associated with achieved schooling. As school achievement is associated with later income [16], an association of duration of breastfeeding with later income is expected. On the other hand, it is important to evaluate the consequences of the small gain in IQ that have been observed among subjects who have been breastfed. In this review, we identified two studies that estimated the impact of breastfeeding on earning ability. In a cohort that has been prospectively followed since birth in a southern Brazilian city, Victora *et al.* [10] reported that duration of breastfeeding was positively associated with IQ, achieved schooling and income at 30 years of age. Those subjects who had been breastfed for 12 months or more had an IQ 3.76 points (95% CI: 2.20; 5.33) higher than those who were breastfed for less than 1 month, and income at 30 years was 341 Brazilian reais (95% CI: 93.8; 588.3) higher among those breastfed for at least 12 months, or 20% of the average income level in the studied population. In addition, mediation analysis showed that IQ in adulthood captured most of the association between breastfeeding and income, that is IQ is mediating the association between breastfeeding and earning ability in adulthood.

In the British Avon Longitudinal Study of Parents and Children, Straub *et al.* [17▪] observed that at 16 years of age, the odds of gaining five General Certificate of Secondary Education (GCSE) passes at a high grade was 1.72 (95% CI: 1.46; 2.05) times higher among those subjects who had been breastfed for at least 6 months, in relation to those who never breastfed, even after controlling for several confounding variables. Based on estimates of lifetime income according to GCSE grades, Straub *et al.* [17▪] predicted that the economic impact of breastfeeding for at least 6 months would be £8799 per child. In terms of economic impact on the society, it was estimated that in a birth cohort of 800 000 child, an increase by 1% in breastfeeding rates would be associated with a gain higher than £33.6 million over the working life of the entire cohort.

CONCLUSION

Concerning the quality of the evidence, in the review on the association between breastfeeding and performance in intelligence tests, we excluded several studies as they failed to control for confounding by socioeconomic and demographic variables, and self-selection bias. These methodologic issues should be taken into consideration in the design and analysis of new studies. The new evidence identified in the review reinforce the hypothesis that breastfeeding has long-term consequences on performance in intelligence tests. Furthermore, this positive association between breastfeeding and development also has consequences on human capital and earning ability.

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Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
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