The Science of Breastfeeding and Brain Development

Mandy Brown Belfort

Introduction

IN ADDITION TO SHORT-TERM benefits such as reduced gastrointestinal infections and pneumonia,¹ the long-term benefits of having been breastfed in infancy are of great interest to clinicians, policy-makers, and individuals faced with personal decisions about how to feed their infants. Because the newborn infant brain is uniquely sensitive to nutrition and to other aspects of the environment,^{2,3} interventions to promote optimal brain development early in life can have lasting effects on neurodevelopmental function. Rigorously designed research on the topic of breastfeeding and neurodevelopment is therefore critical to informing evidence-based policies that promote optimal child development across the life course.

Breastfeeding and Neurodevelopmental Outcomes

Numerous studies to date have tackled the important question of breastfeeding in infancy and the extent to which it enhances a child's cognitive functioning later in life. Most studies on this topic are observational, so a key factor in study design is in measuring and adjusting for shared determinants (confounders) of breastfeeding and neurodevelopmental outcome. Experimental study designs (randomized trials) are challenging to carry out, but have many advantages over observational designs. Overall, there is substantial evidence to support a causal effect of breastfeeding on childhood cognition,^{4,5} but not on other aspects of neurodevelopment such as social-emotional functioning or behavior. The next two paragraphs summarize the design and results of two studies-one observational and one experimental-that contribute evidence in support of policies to promote more prolonged exclusive breastfeeding based on benefits to child intelligence.

In Project Viva, a U.S. longitudinal prebirth cohort that enrolled pregnant women and their infants from 1999 to 2002, we quantified breastfeeding during infancy for ~1,300 fullterm (>37 weeks' gestation) children in two ways: (1) the duration of any breastfeeding to 12 months and (2) the duration of exclusive breastfeeding (no formula) to 6 months. We then assessed several aspects of neurodevelopment at 3 and 7 years, including language, intelligence, visual motor ability, social– emotional development, behavior, and executive function. We found that even after controlling for factors such as socioeconomic status, parental education, maternal IQ, and the home environment, breastfeeding for a longer duration—and especially exclusive breastfeeding for a longer duration—was associated with higher child IQ at school age. Specifically, for each additional month of exclusive breastfeeding, child verbal IQ was 0.8 points higher, translating to a benefit of almost 5 points over 6 months, the recommended duration of exclusive breastfeeding.⁶ However, we did not observe a similar benefit for other outcomes, including parent- and teacher-reported social–emotional or executive function.⁷ Overall, our research supports the hypothesis that breastfeeding promotes greater verbal intelligence in childhood, but we did not see evidence for effects on other aspects of neurodevelopment.

Even the most carefully designed observational studies are limited by the potential for unmeasured confounding to bias results. In other words, even with adjustment for variables such as socioeconomic status and maternal IO, it is possible that the observed relationship between breastfeeding and child cognition may not be due to breastfeeding itself, but by other factors related both to breastfeeding and child outcome. Randomized trials can overcome this limitation, but are challenging to conduct because breastfeeding is a personal choice; it is of course unethical for a researcher to randomly assign an individual mother to breastfeed her infant (or not). The Promotion of Breastfeeding Intervention Trial (PROBIT) was a cluster randomized trial in which 31 maternity hospitals and affiliated outpatient clinics in the Republic of Belarus were randomly assigned in 1996-1997 to implement practices modeled after the Baby-Friendly Hospital Initiative (intervention) or continue with routine maternity care (control). The intervention was successful; at 3 months of age, 43% of infants were exclusively breastfed compared with 6% in the control group.⁸ Testing of almost 14,000 children at early school age (6.5 years) revealed a 7.5-point verbal IQ advantage in the intervention group,⁹ but no effect on social-emotional outcomes or child behavior.¹⁰ Overall, PROBIT provides strong evidence for a cause-andeffect relationship between longer more exclusive breastfeeding and child neurodevelopment, specifically verbal IQ.

Human Milk and Preterm Infant Brain Development

Although studies of breastfeeding in full-term infants provide compelling evidence for a beneficial effect on neurodevelopment, results from those studies may not apply to very preterm infants (<32 weeks' gestation), who are born at an earlier stage of brain development,¹¹ have greater nutritional demands,¹² and are at higher risk for neurodevelopmental impairments.¹³ After birth, preterm infants typically spend several months in the hospital and due to their immaturity are fed not at the breast or by bottle, but instead through a feeding tube. Studies specifically focused on hospitalized preterm infants are needed to determine the extent to which

Department of Pediatric Newborn Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.

feeding breast milk rather than formula promotes more optimal neurodevelopment and reduces burdensome impairments after neonatal intensive care unit (NICU) discharge.

Several studies have described beneficial effects of breast milk rather than formula feeding on neurodevelopmental outcomes in preterm infants, but firm conclusions from most studies are difficult due to small sample sizes and/or inadequate control for confounding factors.¹⁴ Another key factor is the age at which outcomes are measured because assessment in late infancy (e.g., ~18–24 months) may be too early to detect important effects on cognitive function, whereas due to logistical challenges, very few studies have followed large cohorts of preterm infants to school age when more informative cognitive testing is possible.

In a longitudinal study of 180 Australian infants born at <30 weeks' gestation, we examined the relationship between breast milk intake in the first month of the NICU hospitalization and cognitive function at ages 2 and 7 years. Advantages of our study included high (80%) follow-up to school age and detailed cognitive testing. We did not find statistically significant associations of previous breast milk intake during the NICU stay with motor or cognitive development at age 2. However, at age 7, we found that greater breast milk intake was associated with higher IQ and better mathematical ability and working memory. Furthermore, the size of the effect was substantial such that for each additional week that breast milk intake was >50% of the total intake (e.g., predominant breast milk feeding), IQ was 3.5 points higher.¹⁵ Even if residual confounding explains some of this relationship, it is nonetheless a clinically significant effect. Furthermore, on brain magnetic resonance imaging at termequivalent age, previous breast milk intake was associated with larger deep nuclear gray matter volumes; structures in this region include the thalamus and hippocampus, which are major relay stations in the brain.

Providing enough breast milk for their hospitalized preterm infants is often challenging for mothers. An important question for clinicians is what to feed these infants when their own mother's milk is in short supply or not available. A recently published randomized trial addressed this question, and the results provide some insight into the role of breast milk in promoting preterm infant brain development. In the Donor Milk for Improved Neurodevelopmental Outcomes (DoMINO) study, 840 infants born <1,500 g were randomly assigned to receive pasteurized donor milk or preterm formula as a supplement (when needed) to their own mother's milk. As predicted, the rate of necrotizing enterocolitis (NEC)-a life-threatening gastrointestinal condition-was lower in infants who received the donor milk supplementation. Cognitive, language, and motor scores at 18 months were not statistically different between groups, but the percent of infants with cognitive impairment (Bayley scales score <85) was higher in the donor milk group (27% versus 16%).¹⁶ These results suggest that despite its protective effects against NEC, donor milk may not be as beneficial as maternal milk for preterm infant brain development.

Mechanisms Linking Breastfeeding with Brain Development

Maternal milk feeding is common to all mammals and allows for the continued transfer of resources from mother to infant (e.g., nutritional, immune).¹⁷ The infant brain undergoes rapid development in the first year of life, and this development is strongly influenced by nutritional factors. Thus, the beneficial effects of breastfeeding on the infant brain may be explained by nutrients or even non-nutrient bioactive factors that are present in breast milk, but absent in infant formula. Notably, research to identify specific components of breast milk that are responsible for its beneficial effects on the developing brain has been disappointing.^{18,19}

Another important effect of maternal milk feeding is to extend the period of maternal care. An infant's brain development is influenced by interactions with the environment, particularly mother-infant interactions. For example, breastfeeding mothers appear to spend more time engaged in emotional care than mothers who feed their infants formula.²⁰ Thus, it is possible that breastfeeding is beneficial to the developing brain not just through nutritional effects but also due to differences in mother-infant interactions. The finding in preterm infants that donor milk does not appear to benefit neurodevelopment-whereas maternal milk feeding doesprovides some support for this hypothesis; mothers who provide their own milk may be more engaged in other ways with their infant, and this engagement with the mother could explain differences in infant brain development independent of nutritional aspects of maternal milk.

Conclusion

In both full-term and preterm populations, evidence is compelling that breastfeeding or maternal milk feeding benefits child neurodevelopment. These benefits may result from nutritional differences in breast milk compared with infant formula and differences in maternal–infant interactions may also be at play. Overall, available evidence regarding neurodevelopmental benefits supports existing recommendations that infants should be breastfed exclusively for 6 months and that hospitalized preterm infants should receive fortified maternal milk.²¹ More work is still needed to elucidate mechanisms behind these beneficial effects and to ensure that mothers and infants are well supported in following recommendations.

Disclosure Statement

No competing financial interests exist.

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Address correspondence to: Mandy Brown Belfort, MD, MPH Department of Pediatric Newborn Medicine Brigham and Women's Hospital Harvard Medical School 75 Francis Street Boston, MA 02115

E-mail: mbelfort@bwh.harvard.edu