Neurodevelopmental Outcomes of Preterm Infants Fed Human Milk

A Systematic Review

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KEYWORDS

• Human milk • Neurodevelopmental • Brain • Donor milk • Outcomes

KEY POINTS

- Human milk (HM) contains the precursors of the n-3 and n-6 long-chain polyunsaturated fatty acids (LC-PUFA), especially docosahexaenoic acid and arachidonic acid, which play an important role in neurogenesis.
- Preterm infants derive a developmental benefit from HM.
- There is evidence to support the beneficial effects of HM on brain, visual, and cognitive development from infancy to adolescence.
- Volume of breast milk consumed is an important predictor of cognitive outcomes.

This article covers the benefits contributing to improved neurodevelopmental outcomes. A systematic evaluation of peer-reviewed studies published in PubMed was conducted. Terms of interest were prematurity, human milk (HM), donor milk benefits, neurodevelopmental outcomes, and brain.

There have been several recent papers summarizing the importance of nutrition for early brain development and developmental outcomes.[1,2] Although the evidence for the association of HM and improved medical outcomes[3,4] is clear, the relationship with neurodevelopmental outcomes has at times been controversial, and it has been implied that improved outcomes are related more to higher maternal education and socioeconomic status rather than nutrients found in HM.[5] The evidence is clearer for preterm infants with randomized trials demonstrating decreased rates

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of sepsis and necrotizing enterocolitis and 2 weeks shorter duration of care in the neonatal intensive care unit (NICU).[4,6–8] Because these neonatal morbidities are associated with adverse neurodevelopmental outcomes, this is one mechanism by which the use of HM is associated with improved neurodevelopment in the premature infant. There is additional evidence, however, that HM is associated with more optimal brain development. HM contains the n-3 and n-6 fatty acids linolenic acid and linoleic acid, which are precursors of the n-3 and n-6 long-chain polyunsaturated fatty acids (LC-PUFA). LC-PUFAs, especially docosahexaenoic acid (DHA) and arachidonic acid (AA), play an important role in neurogenesis. Evidence for the benefit of supplementation with LC-PUFA prenatally and in formula, however, is inconclusive.[9–12]

There are emerging studies, however, supporting the effects of HM on brain development. Deoni and colleagues[13] used MRI to assess white matter microstructure of 133 children between 10 months and 4 years of age who were either exclusively HM fed a minimum of 3 months, exclusively formula fed, or received a mixture of HM and formula. They identified that HM-fed children exhibited increased white matter development in later maturing frontal and association brain regions and found positive associations between white matter microstructure and breastfeeding duration in several brain regions. They also reported higher receptive language scores and vision reception scores among the infants exclusively breast fed. Isaacs and colleagues,[14] using MRI and long-term follow-up, reported in a group of 50 adolescents that percent expressed HM was associated with higher verbal intelligence for the cohort, and for boys with all intelligence quotient (IQ) scores, total brain volume and white matter volume. Their study supports the beneficial effects of HM on brain and cognitive development. Kafouri and colleagues[15] showed that exclusive breastfeeding was associated with increased cortical thickness of the superior and inferior parietal lobules and breastfeeding was associated with variations in the thickness of the parietal cortex in a sample of 512 adolescents. They also reported an association of breastfeeding duration with full scale and performance IQ at ages 12 to 18 years.

This article focuses on neurodevelopmental outcomes in preterm infants fed HM. Discussed are the components of breast milk and their role in neurodevelopment, studies of outcomes during infancy, childhood and adolescence, the role of maternal and infant nutritional supplementation during breastfeeding, and the challenges of studying the role of breastfeeding and breast milk provision in neurodevelopmental outcomes.

COMPONENTS OF BREAST MILK AND NEURODEVELOPMENT

The mechanisms by which breast milk contributes to improved neurodevelopmental outcomes have not yet been fully explored. Components of HM that have received significant attention are LC-PUFA. These components have been implicated in improved cognitive[16] and visual development[17] in infants.

Another, more recent, emerging body of evidence suggests that HM oligosaccharides, (the HM “glycobiome”) support the establishment of a healthy neonatal gut microbiome.[18] In turn, necrotizing enterocolitis, which is a risk factor for poor neurodevelopmental outcomes in premature infants,[19] is associated with abnormal neonatal gut microbiome, or “dysbiosis.”[20,21] Thus, although there is no direct evidence linking HM oligosaccharides to neurodevelopmental outcomes in preterm infants, a case is made for their indirect contribution to improved cognitive outcomes via the necrotizing enterocolitis pathway.