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Review

Human Milk and Brain Development in Infants

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Abstract: Human milk is considered the most advantageous source of nourishment for infants. Even though there is no ideal composition of human milk, it still contains a unique combination of components that contribute to brain development. The aim of this review is to provide an overview on the possible correlation of human milk with the neurodevelopment of infants, with a special emphasis on myelination and epigenetic modifications. Research in human milk is a rapidly expanding field and cutting-edge technologies might contribute to identify specific mechanisms underlying the beneficial effects on human milk on neurodevelopment.

Keywords: human milk; neurodevelopment; macronutrients; sialic acid; micronutrients; bioactive components; preterm infants; epigenetic modifications

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1. Introduction

Breastfeeding and human milk (HM) are the regulatory standards for newborn feeding. The American Academy of Pediatrics recommends exclusive breastfeeding for the first 6 months, followed by another year or longer of breastfeeding in combination with the introduction of complementary foods [1]. Previous research has shown that human milk, as well as the act of breastfeeding, induce both short-term benefits such as optimal colonization of the intestinal microbiome, protection against infectious diseases, decreased infant mortality from all causes, and long-term benefits such as the reduced risk of obesity and type 2 diabetes, and improved cognitive performance [2–4]. HM contains a unique combination of components. In addition to classes of macro- and micronutrients such as carbohydrates, proteins, lipids, and vitamins, minerals, respectively, HM contains a large range of bioactive components such as growth factors, hormones, antimicrobial components, digestive enzymes, transporters, and maternal cells (e.g., stem cells, leucocytes). HM, therefore, is dynamic in that its composition is continuously changing throughout lactation to meet the infant's needs during growth and development. In addition, the composition of milk differs between mothers who gave birth at term and those who delivered prematurely. Moreover, many studies have shown that HM helps the neurodevelopment of both term and preterm babies and these benefits may stem from the different composition of HM compared to artificial infant formula [5,6]. However, most of the studies in this field are association studies, and hence the possible beneficial underlying mechanisms have to be identified. The aim of this review is to summarize the current knowledge on the

composition of human milk and its changes in the stages of breastfeeding, describing the differences in the composition of HM for full-term and pre-term infants. In addition, based on current knowledge, we have provided an overview of the possible correlation of HM components with the neurodevelopment of the infants, describing all HM components that might be involved in this process. Moreover, further studies are needed to identify specific mechanisms of action of components of human milk involved in the neurodevelopment of the infants.

2. Human Milk Composition

HM is characterized by its optimal adaption in composition to infant needs providing nutritional and bioactive factors [7]. The variations in the HM composition are dependent on lactation stage, gestation, maternal diseases, and diet [8–10]. HM is made up of 87% water and the rest consists mainly of macronutrients such as carbohydrates, proteins and lipids [5,11].

2.1. Bioactive Components in Human Milk

In addition to the nutritional components, there are many bioactive components in HM such as antimicrobial factors, cytokines and anti-inflammatory substances, hormones, growth modulators and digestive enzymes, which influence biological processes or substrates, playing an important role in the health of the infants. Due to the immaturity of the digestive and immune system, these components have an important role, especially in neonatal life [12,13]. Among the bioactive components, breast milk is rich in miRNAs, small non-coding RNA that within membranous vesicles, such as exosomes, are present in body fluids and can mediate intracellular communication. Many studies have revealed that breast milk miRNAs, through the infant's systemic circulation, can perform tissue-specific immunoprotective and developmental functions in a newborn. However, it is not yet clear how these miRNAs are metabolized and especially how they act in the gene regulation of the infant [14,15].

2.2. Variation in Human Milk Composition According to the Lactation Stage

HM is a dynamic and bioactive fluid that varies between mothers. Furthermore, its composition varies according to the lactation stage and between preterm and term breast milk [16,17]. The first form of milk produced in the early days after birth is colostrum. It is rich in secretory IgA, lactoferrin, lysozyme and leukocytes, growth factors, vitamins and minerals, indicating that its primary functions are immunological and trophic [16,18,19]. Consequently, with the production of transition milk, the lactose concentration increases. The activation time of milk secretion is different among women, but generally occurs in the first three days after childbirth. A delayed onset can occur in the event of preterm birth or caesarean section. Transitional milk has some characteristics of colostrum, but can support the nutritional and developmental needs of the rapidly growing baby. After five days to two weeks after giving birth, the milk will be considered largely mature. After the first month of life, HM will not undergo significant changes in its composition.

3. Macronutrients in Human Milk Involved in Neurodevelopment

HM contains macro- and micronutrients that are essential during the neonatal period [20].

Lactose, a disaccharide and an excellent source of slow-release energy is the main carbohydrate in HM and seems to exert modeling effects on the intestinal microbiota and promote brain development [21].

Proteins act as nutritional support and as carriers of other nutrients. The most abundant proteins are casein, α-lactalbumin, lactoferrin, secretory immunoglobin A (IgA), lysozyme and serum albumin. Non-protein compounds of HM such as urea, uric acid, creatinine, amino acids and nucleotides comprise about 25% of nitrogen.

The main energy source in HM is **lipids**, providing polyunsaturated fatty acids (PUFA), fat-soluble vitamins, complex lipids and bioactive compounds. The composition of HM fatty acids, especially long-chain polyunsaturated fatty acid (LCPUFA), is widely influenced by the maternal diet. The omega-6 fatty acid (linoleic acid) and the omega-3 fatty acid (α-linolenic acid) are dietary precursors of LCPUFA and most abundant HM fat. LCPUFAs include docosahexaenoic acid and arachidonic acid, which are involved in important physiological processes such as growth and immune response and are critical for brain development [22–25]. The nutritional quality of HM is highly preserved; however, the maternal diet and body deposits can modify many micronutrients in HM. An inadequate supply of some micronutrients appears to have a negative impact on brain structure or function [26].

3.1. Human Milk Oligosaccharides

Among the components of HM, oligosaccharides (HMOs) are the third most abundant components after lipids and lactose, and differ significantly between HM and infant formula in concentration [27]. These simple sugar polymers that are mainly digested by the colon flora, play important functions, in particular, the modulation of the intestinal microbiota composition, influencing a large number of physiological processes of the infants [16,28–30]. Furthermore, it is interesting to note that HMOs can supply fucose (Fuc) and sialic acid (SA), which seem to play an important role in brain development [31]. Glucose, galactose, N-ethylglucosamine, Fuc, and SA are the five basic monosaccharides that make up HMOs. SA-rich HMOs have been hypothesized to be involved in learning and memory [32]. Most HMOs can be synthesized de novo by the mother and transferred to the fetus through the umbilical cord or later via breast milk. The HMO concentration is mainly influenced by the maternal genetic background and diet [33]. Austin et al. recently showed that at equivalent lactation stage and post-menstrual age the composition of the preterm and the term breast milk differs in HMO concentration. Preterm milk showed a reduced concentration of HMOs containing α-1,2-linked Fuc during the first month after birth and a higher concentration of 3′-sialyllactose [6,7]. Since HMOs are absent in infant formula, causing newborns not to receive the same health benefits as breastfed infants, a mixture of galactooligosaccharides (GOS) and fructoligosaccharides (FOS), also called inulin, has been developed and is added to certain products. Inulin is known to be bifidogenic, which imitates breast milk prebiotics. GOS and FOS can help modulate the immune system, reducing the incidence of infections, but further studies are needed to clarify the specific effects of GOS and FOS [33].

3.2. Sialic Acid Is Involved in Brain Development

The SA content in breast milk is 0.3–1.5 mg/mL. SA can be obtained from the diet or produced de novo. Further, it can be found in different sialoglycoconjugate compounds such as oligosaccharides, glycolipids and glycoproteins. Only a very small amount of SA is in free form. Among the oligosaccharides containing SA molecules, the most abundant is sialyllactose (SL). SL is composed of a SA molecule bound to lactose and can exist in two isoforms, 3′-SL and 6′-SL, depending on the position of the linkage between SA and lactose. In the human body, the highest SA concentration is found in the brain as N-Acetylneuraminic acid, where it is an integral part. In the last year, some studies have found that SL can influence the brain development of the newborn, while SA conjugated with glycolipids and glycoproteins plays an important role in synapse formation and neural transmission [34,35]. Conjugant sialic oligosaccharide concentration in human colostrum undergoes marked changes in the first 3 days of lactation, following the physiological needs of newborns [36], demonstrating the importance of dynamic changes in the composition of maternal milk for brain development. Neurological development by magnetic resonance imaging was analyzed in pig models and Mudd et al. showed that the development of the corpus callosum, prefrontal cortex, and hippocampus seems to be influenced by dietary supplementation of SA in the form of SL [34]. The different SL isomers are involved in

the brain and microbiome development of neonatal piglet models. SL introduced with the diet could play a dual role in supporting the optimal growth and brain development of the newborn [37]. The SA level expressed in HM is influenced by a variety of factors such as genetics, geographic regions and maternal diet and is higher compared to infant formula based on bovine milk [38]. Wang et al. compared the SA concentration in the frontal cortex of 25 infants who died of sudden infant death syndrome by using high performance liquid chromatography. Their data showed a higher SA concentration in HM-fed infants as opposed to infants fed with formula, suggesting an increase in synaptogenesis and differences in neurodevelopment [39]. Obelitz-Ryom et al. studied the effects of SL supplementation in milk on neurological development in preterm pigs. Dietary supplementation with SL induces positive functional brain effects and increases the expression of genes related to SA metabolism, myelination and ganglioside biosynthesis in the hippocampus at 3 weeks of age, suggesting that SL may represent an important supplement for infant formula to promote the development of the preterm neonatal brain [40]. Further studies are needed to confirm the involvement of SA in the neurodevelopment of newborns and the mechanisms involved in the process of brain development. Identifying the specific "effects" of HM components on infant brain development is currently a complex research field. Several confounding variables may limit the research in this field. Most of this research relies, indeed, on correlational studies (since breastfeeding cannot be randomly assigned in a true experimental/randomized trial) or on animal studies, which have limited translational potential to humans.

4. Micronutrients in Human Milk Involved in Neurodevelopment

Iron, folate and zinc have a critical role in brain development and function. The concentrations of these micronutrients in HM are relatively unaffected by maternal intake. An iron deficiency can lead to hypomyelination, permanent deficiency in the number of dopamine receptors and worsening of neurotransmission. Total HM iron concentrations reach a maximum in colostrum and subsequently decrease during the first year of lactation; after 6 months of age, iron supplementation has been recommended because the concentrations in HM are insufficient for infant requirements [41]. The predominant form of folate in HM is 5-methyltetrahydrofolate; its concentration is low in colostrum with progressive increase after childbirth, reaching a peak at 2–3 months and then remaining stable [30]. Zinc concentrations in HM decrease abruptly from colostrum to transitional milk, followed by a gradual reduction during lactation. Zinc deficiency appears to affect cognitive development [41,42].

Choline is an essential micronutrient for the development of the fetus and newborn. It is the precursor of many important compounds such as phospholipid, phosphatidylcholine, and sphingomyelin membranes, and a precursor of the acetylcholine neurotransmitter. Choline deficiency leads to persistent cognitive and memory deficits [43]. Breast milk choline concentrations increase between 7 and 22 days postpartum and remain stable in mature milk [44].

Iodine is a micronutrient that plays a vital role in the production of thyroid hormone (TH); a severe iodine deficiency is associated with mental retardation in newborns. Pregnant women are prone to iodine deficiency due to the double iodine requirement during pregnancy. Iodine concentrations reach a maximum in colostrum, and then decrease over the next few weeks until they reach a plateau at 100–150 μg/L in mature milk. The use of iodized salt during breastfeeding allows the transfer of adequate amounts of iodine to newborns through mother's milk, preventing iodine deficiency [45].

Calcium plays a vital role as a second messenger in signal transduction, which controls the production of neurons and glial cells. Total calcium concentrations in breast milk increase abruptly in the first 5 days of breastfeeding and then gradually decrease throughout breastfeeding [41].

Vitamin B-6 is an essential cofactor for more than 100 enzymes involved in amino acid metabolism, glycolysis, and gluconeogenesis. Vitamin B-6, especially in form of pyridoxal,

increases in the first few weeks postpartum, followed by a gradual decline in late lactation; after 6 months of age, supplementation of Vitamin B-6 is needed because the concentration in human milk appears insufficient for infants' vitamin B-6 requirements. Deficiency of vitamin B-6 is associated with neurological and behavior abnormalities [46].

Vitamin B-12 plays a fundamental role in the preservation of the myelin sheath around neurons and the synthesis of neurotransmitters, and its deficiency can cause damage to the myelin sheath leading to syndromes such as myelopathy, neuropathy, and neuropsychiatric disorders. The total concentration of vitamin B-12 in breast milk decreases at the beginning of lactation, then remains stable for up to 12 weeks and then slowly decreases [26,41].

Vitamin C plays an important role in developing neurons through their maturation and differentiation, and in forming myelin. The total concentration of ascorbic acid (AA) in breast milk is greater in colostrum and decreases during lactation depending on the difference in maternal status and food intake [26,41].

Vitamin D plays an important role in brain development, inducing the nerve growth factor (NGF), promoting neurite growth, and inhibiting neuronal apoptosis in the hippocampus [26]. The levels of vitamin D, regardless of the maternal diet, are low, suggesting a necessary supplementation of vitamin D to the infants [16,47].

Detailed concentrations of micronutrients in human milk are shown in Table 1.

Table 1. Micronutrient concentration in human milk.

Micronutrient	First Weeks of Lactation		References
	Preterm Group	Term Group	
	33 w (27–37 w)	40 w (39–41 w)	
	(Mean ± SD)	(Mean ± SD)	
Iron [mg/L]	1.35 ± 0.42	1.02 ± 0.37	[48–50]
Folate (Vitamin B-9) [ng/mL]	21 ± 14	30.4 ± 10	[51]
Zinc [mg/L]	2.25 ± 0.95	2.6 ± 1.1	[48,52,53]
Choline [mg/L]	158 ± 10	258 ± 10	[53,54]
Iodine [mg/L]	0.092 ± 0.67	0.087 ± 0.41	[48]
Calcium [mg/L]	289 ± 25	279 ± 30	[48,55,56]
Vitamin B-6 [ng/mL]	33 ± 0.30	53 ± 0.40	[46,51]
Vitamin B-12 [ng/mL]	0.55 ± 0.11	0.33 ± 0.20	[46,51]
Vitamin C [mg/L]	53 ± 18.7	45 ± 15.8	[57–59]
Vitamin D [ug/L]	1.36 ± 0.16	0.86 ± 0.10	[60]

5. Differences in the Composition of Human Milk for Full-Term and Pre-Term Babies: Effects on Neurodevelopment

In the first weeks following birth, preterm breast milk is richer in proteins, free amino acids, fats and sodium than term breast milk. On the contrary, the calcium level is lower in preterm milk and does not increase over time, while copper and zinc levels are higher at the beginning of breastfeeding and then decrease. Levels of other minerals appear to be the same in both preterm and term breast milk. Another difference in term milk is in the content of oligosaccharides, which is highly variable in preterm milk; moreover, preterm milk is richer in glycosaminoglycans than term milk. Finally, differences in bioactive molecules are observed mainly in colostrum and subsequent milk and not in mature milk [31,61]. Many studies have shown that preterm infants have different nutritional needs than term-born infants. Apart from the possibility of developing NEC and sepsis or failure to grow, preterm infants are at greater risk of poor neurodevelopment, showing alterations in the size of the brain, its structure, connectivity and function. Factors that influence neurodevelopmental

outcomes include gestational age, birth weight, neonatal morbidities such as brain injury and infections, pre- and postnatal growth, and nutrition [31]. Even though breast milk is high in proteins, bioactive molecules and various other essential molecules it alone does not provide optimal nutrition for premature babies. The infants need an adequate fortification of HM to satisfy the nutritional requirements for growth and development. Despite fortified human milk providing short and long-term benefits for premature babies, this can also have complications because the use of fortifying agents is associated with an increase in oxidative stress markers as well as bacterial contamination infections associated with high mortality rates [62].

6. Human Milk Components Influence Myelination

Nutrition in infants plays a fundamental role in the first period of life, which coincides with brain growth and the development of cognitive, behavioral, and socio-emotional functions [63]. During this period, the eloquent cortex network is shaped and refined through processes including myelination, dendritic arborization, synaptogenesis and synaptic pruning [64]. Myelination, the development of myelin surrounding neural axons, is essential for optimal brain function [65]. Myelin is a lipid-rich insulating substance which ensures the proper transmission of the nerve impulses and provides an appropriate environment for the survival of axons [66]. In the central nervous system, oligodentrocytes produce myelin [67]. Nutrients, such as short- and long-chain PUFAs, phospholipids, neurotrophic factors, biofactors, hormones and micronutrients, can influence myelination by altering the building block compositions needed for myelin membrane production [68]. Therefore, deficiencies of these nutrients can significantly alter myelination, disrupting normal brain function and compromising cognitive outcomes in the newborn [63]. With specific reference to brain myelination, breast milk is an important source of long-chain PUFAs, including docosahexaenoic and arachidonic acid (DHA and ARA), that together comprise more than 20% of the brain's fatty acid content [69], and phospholipids such as phosphatidylcholine that make up 10% of the lipid weight of myelin. Approximately 40% of the lipid content of mature human milk is sphingomyelin [70], a sphingolipid that plays a critical role in the development of the myelin sheath [71,72]. HM is also an important source of cholesterol, which is essential for myelin synthesis [73]. Mothers' hormones, such as thyroid hormone T3, acting through the nuclear receptors, control the expression of genes involved in myelination, cell differentiation, migration, and signaling [74,75]. Brain magnetic resonance imaging (MRI) studies have shown that infants fed with HM exhibited greater white matter development; and a positive association between the microstructure of the white matter in many brain regions and the duration of lactation [63,76,77]. Furthermore, these infants showed an increase in verbal and non-verbal cognitive skills as compared to partially or exclusively formula-fed infants [6,78]. The improvement of cognitive skills might correlate to neuro-associated nutrients such as long-chain polyunsaturated fatty acids, phosphatidylcholine, sphingomyelin and oligosaccharides, which are found in HM [79,80]. The importance of HM in brain development was further confirmed through the proliferation and differentiation of oligodendrocytes and their positive effect on myelination [80].

7. Epigenetic Modifications and Human Milk: The Role of MicroRNAs in Brain Development

MicroRNAs (miRNAs) are small RNA molecules, ~20–24 nucleotides long, that can negatively control their target gene expression post-transcriptionally. There are currently more than 460 human miRNAs known, and the total number is predicted to be much larger. miRNAs play pivotal roles in regulating diverse developmental processes by targeting mRNA for translational repression, cleavage, or destabilization. Several studies have demonstrated that miRNA is present in whole HM, including within milk fat globules [81]. HM seems to have an important role in the modulation of gene expression and therefore in the health of the newborn [82]. Recent studies show that HM plays a transmitter role between the lactation mother genome and the epigenetic regulation of newborn genes [81].

Epigenetic studies showed possible effects of nutrients on gene expression and therefore epigenetic processes are associated with the beneficial effects of breast milk on health. The epigenome can be easily shaped by environmental factors during the perinatal period. In particular, after fertilization most of the genome can undergo active and passive demethylation followed by de novo methylation, influencing the epigenetic landscape [83]. Many studies have shown the impact of feeding on newborns, influencing the expression of genes with short- and long-term effects on the organism. DNA methylation, histone modification, chromatin remodeling and miRNAs are among the main epigenetic processes [82–84]. The miRNAs in HM play a key role in the upregulation of genes involved in development such as FTO, INS and IGF1, providing adequate epigenetic programming of the infant, compared to the infant formula which, on the contrary, has a low level of miRNA. The miRNAs are secreted as extracellular vesicles derived from the epithelial cells of the mammary gland and transported in exosomes (nanoparticles of 30–100 nm) surrounded by a rigid double-layer lipid membrane that protects against the harsh conditions present in the gastrointestinal tract and guarantees the transfer of miRNA to the systemic circulation of the newborn. miRNA-148a-3p appears to be the most abundant miRNA detected in breast milk. It targets DNA methyltransferase 3b (DNMT3B) and during the development of the infant, it suppresses the expression of DNMT3B, inhibiting de novo-DNA methylation, influencing the development in the infant [14,81]. Numerous studies have shown that miRNAs are long-range gene regulators and can promote brain development and its functions, suggesting a role in neurodevelopment [85–87]. Moncini et al. have shown that miR-103 and miR-107 (detected in HM) are able to regulate the cyclin-dependent kinase 5 (CDK5) regulatory subunit 1, which codes for p35, the main activating subunit of CDK5 involved in brain development and function [88]. Munch et al. hypothesized that miR-118.2 in breast milk targets a family of proteins (odd Oz/ten-m homolog 2) widely present in the central nervous system, in particular on the brain axons, and seems to be involved in cell–cell communication, suggesting a miR-118.2 action in nervous system pathways and brain development [89]. However, further studies identifying breast milk miRNAs involved in infant neurodevelopment and their mechanisms of action are necessary.

8. Conclusions

Human milk is the extraordinary product of 200 million years of symbiotic coevolution between a mammalian and its infant [90]. In the last 15 years, research in the field has dramatically grown and it is fast evolving. The first discovery on the stem cells in HM was in 2007 [91], 261 proteins never before identified were identified in the proteome of HM in 2009 [92], while 300 new microRNA molecules were characterized in 2015 [14]. Furthermore, it was found that the milk microbiome, until recently considered without physiological relevance, is characterized by a microbial community which interacts with the intestinal microbiome [93–95]. These stunning discoveries strengthen the critical role of HM in early life nutrition and broaden its transgenerational impact on infant health.

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References

1. Section on Breastfeeding. Breastfeeding and the use of human milk. *Pediatrics* **2012**, *129*, e827–e841. [CrossRef]
2. Young, B.E. *Breastfeeding and Human Milk: Short and Long-Term Health Benefits to the Recipient Infant*; Elsevier: Amsterdam, The Netherlands, 2017.

3. Marild, S.; Hansson, S.; Jodal, U.; Oden, A.; Svedberg, K. Protective effect of breastfeeding against urinary tract infection. *Acta Paediatr.* **2004**, *93*, 164–168. [CrossRef] [PubMed]
4. Hassiotou, F.; Hepworth, A.R.; Metzger, P.; Tat Lai, C.; Trengove, N.; Hartmann, P.E.; Filgueira, L. Maternal and infant infections stimulate a rapid leukocyte response in breastmilk. *Clin. Transl. Immunol.* **2013**, *2*, e3. [CrossRef] [PubMed]
5. Martin, C.R.; Ling, P.R.; Blackburn, G.L. Review of Infant Feeding: Key Features of Breast Milk and Infant Formula. *Nutrients* **2016**, *8*, 279. [CrossRef]
6. Austin, S.; De Castro, C.A.; Sprenger, N.; Binia, A.; Affolter, M.; Garcia-Rodenas, C.L.; Beauport, L.; Tolsa, J.F.; Fischer Fumeaux, C.J. Human Milk Oligosaccharides in the Milk of Mothers Delivering Term versus Preterm Infants. *Nutrients* **2019**, *11*, 1282. [CrossRef] [PubMed]
7. Mosca, F.; Gianni, M.L. Human milk: Composition and health benefits. *Pediatr. Med. Chir.* **2017**, *39*, 155. [CrossRef]
8. Innis, S.M. Impact of maternal diet on human milk composition and neurological development of infants. *Am. J. Clin. Nutr.* **2014**, *99*, 734S–741S. [CrossRef]
9. Bzikowska-Jura, A.; Czerwonogrodzka-Senczyna, A.; Oledzka, G.; Szostak-Wegierek, D.; Weker, H.; Wesolowska, A. Maternal Nutrition and Body Composition During Breastfeeding: Association with Human Milk Composition. *Nutrients* **2018**, *10*, 1379. [CrossRef] [PubMed]
10. Demmelmair, H.; Koletzko, B. Variation of Metabolite and Hormone Contents in Human Milk. *Clin. Perinatol.* **2017**, *44*, 151–164. [CrossRef]
11. Eriksen, K.G.; Christensen, S.H.; Lind, M.V.; Michaelsen, K.F. Human milk composition and infant growth. *Curr. Opin. Clin. Nutr. Metab. Care* **2018**, *21*, 200–206. [CrossRef]
12. Hamosh, M. Bioactive factors in human milk. *Pediatr. Clin. N. Am.* **2001**, *48*, 69–86. [CrossRef]
13. Nolan, L.S.; Parks, O.B.; Good, M. A Review of the Immunomodulating Components of Maternal Breast Milk and Protection Against Necrotizing Enterocolitis. *Nutrients* **2019**, *12*, 14. [CrossRef] [PubMed]
14. Alsaweed, M.; Hartmann, P.E.; Geddes, D.T.; Kakulas, F. MicroRNAs in Breastmilk and the Lactating Breast: Potential Immunoprotectors and Developmental Regulators for the Infant and the Mother. *Int. J. Environ. Res. Public Health* **2015**, *12*, 13981–14020. [CrossRef] [PubMed]
15. Zhou, Q.; Li, M.; Wang, X.; Li, Q.; Wang, T.; Zhu, Q.; Zhou, X.; Wang, X.; Gao, X.; Li, X. Immune-related microRNAs are abundant in breast milk exosomes. *Int. J. Biol. Sci.* **2012**, *8*, 118–123. [CrossRef]
16. Ballard, O.; Morrow, A.L. Human milk composition: Nutrients and bioactive factors. *Pediatr. Clin. N. Am.* **2013**, *60*, 49–74. [CrossRef]
17. Léké, A.; Grognet, S.; Deforceville, M.; Goudjil, S.; Chazal, C.; Kongolo, G.; Dzon, B.E.; Biendo, M. Macronutrient composition in human milk from mothers of preterm and term neonates is highly variable during the lacta-tion period. *Clin. Nutr. Exp.* **2019**, *26*, 59–72. [CrossRef]
18. Munblit, D.; Peroni, D.G.; Boix-Amoros, A.; Hsu, P.S.; Van't Land, B.; Gay, M.C.L.; Kolotilina, A.; Skevaki, C.; Boyle, R.J.; Collado, M.C.; et al. Human Milk and Allergic Diseases: An Unsolved Puzzle. *Nutrients* **2017**, *9*, 894. [CrossRef]
19. Blesa, M.; Sullivan, G.; Anblagan, D.; Telford, E.J.; Quigley, A.J.; Sparrow, S.A.; Serag, A.; Semple, S.I.; Bastin, M.E.; Boardman, J.P. Early breast milk exposure modifies brain connectivity in preterm infants. *Neuroimage* **2019**, *184*, 431–439. [CrossRef]
20. Czosnykowska-Lukacka, M.; Krolak-Olejnik, B.; Orczyk-Pawilowicz, M. Breast Milk Macronutrient Components in Prolonged Lactation. *Nutrients* **2018**, *10*, 1893. [CrossRef]
21. Romero-Velarde, E.; Delgado-Franco, D.; Garcia-Gutierrez, M.; Gurrola-Diaz, C.; Larrosa-Haro, A.; Montijo-Barrios, E.; Muskiet, F.A.J.; Vargas-Guerrero, B.; Geurts, J. The Importance of Lactose in the Human Diet: Outcomes of a Mexican Consensus Meeting. *Nutrients* **2019**, *11*, 2737. [CrossRef]
22. Demmelmair, H.; Koletzko, B. Lipids in human milk. *Best Pract. Res. Clin. Endocrinol. Metab.* **2018**, *32*, 57–68. [CrossRef]
23. Koletzko, B. Human Milk Lipids. *Ann. Nutr. Metab.* **2016**, *69* (Suppl. S2), 28–40. [CrossRef]
24. Abedi, E.; Sahari, M.A. Long-chain polyunsaturated fatty acid sources and evaluation of their nutritional and functional properties. *Food Sci. Nutr.* **2014**, *2*, 443–463. [CrossRef]
25. Carlson, S.E.; Colombo, J. Docosahexaenoic Acid and Arachidonic Acid Nutrition in Early Development. *Adv. Pediatr.* **2016**, *63*, 453–471. [CrossRef]
26. Gonzalez, H.F.; Visentin, S. Micronutrients and neurodevelopment: An update. *Arch. Argent. Pediatr.* **2016**, *114*, 570–575. [CrossRef] [PubMed]
27. Plaza-Diaz, J.; Fontana, L.; Gil, A. Human Milk Oligosaccharides and Immune System Development. *Nutrients* **2018**, *10*, 1038. [CrossRef] [PubMed]
28. Andreas, N.J.; Kampmann, B.; Mehring Le-Doare, K. Human breast milk: A review on its composition and bioactivity. *Early Hum. Dev.* **2015**, *91*, 629–635. [CrossRef] [PubMed]
29. Witkowska-Zimny, M.; Kaminska-El-Hassan, E. Cells of human breast milk. *Cell Mol. Biol. Lett.* **2017**, *22*, 11. [CrossRef] [PubMed]
30. Milani, C.; Duranti, S.; Bottacini, F.; Casey, E.; Turroni, F.; Mahony, J.; Belzer, C.; Delgado Palacio, S.; Arboleya Montes, S.; Mancabelli, L.; et al. The First Microbial Colonizers of the Human Gut: Composition, Activities, and Health Implications of the Infant Gut Microbiota. *Microbiol. Mol. Biol. Rev.* **2017**, *81*, e00036-17. [CrossRef] [PubMed]
31. Underwood, M.A. Human milk for the premature infant. *Pediatr. Clin. N. Am.* **2013**, *60*, 189–207. [CrossRef]

32. Oliveros, E.; Vazquez, E.; Barranco, A.; Ramirez, M.; Gruart, A.; Delgado-Garcia, J.M.; Buck, R.; Rueda, R.; Martin, M.J. Sialic Acid and Sialylated Oligosaccharide Supplementation during Lactation Improves Learning and Memory in Rats. *Nutrients* **2018**, *10*, 1519. [CrossRef] [PubMed]
33. Wicinski, M.; Sawicka, E.; Gebalski, J.; Kubiak, K.; Malinowski, B. Human Milk Oligosaccharides: Health Benefits, Potential Applications in Infant Formulas, and Pharmacology. *Nutrients* **2020**, *12*, 266. [CrossRef] [PubMed]
34. Mudd, A.T.; Fleming, S.A.; Labhart, B.; Chichlowski, M.; Berg, B.M.; Donovan, S.M.; Dilger, R.N. Dietary Sialyllactose Influences Sialic Acid Concentrations in the Prefrontal Cortex and Magnetic Resonance Imaging Measures in Corpus Callosum of Young Pigs. *Nutrients* **2017**, *9*, 1297. [CrossRef]
35. Nakano, T.; Sugawara, M.; Kawakami, H. Sialic acid in human milk: Composition and functions. *Acta Paediatr. Taiwan* **2001**, *42*, 11–17.
36. Asakuma, S.; Akahori, M.; Kimura, K.; Watanabe, Y.; Nakamura, T.; Tsunemi, M.; Arai, I.; Sanai, Y.; Urashima, T. Sialyl oligosaccharides of human colostrum: Changes in concentration during the first three days of lactation. *Biosci. Biotechnol. Biochem.* **2007**, *71*, 1447–1451. [CrossRef] [PubMed]
37. Jacobi, S.K.; Yatsunenko, T.; Li, D.; Dasgupta, S.; Yu, R.K.; Berg, B.M.; Chichlowski, M.; Odle, J. Dietary Isomers of Sialyllactose Increase Ganglioside Sialic Acid Concentrations in the Corpus Callosum and Cerebellum and Modulate the Colonic Microbiota of Formula-Fed Piglets. *J. Nutr.* **2016**, *146*, 200–208. [CrossRef]
38. Wang, B. Molecular mechanism underlying sialic acid as an essential nutrient for brain development and cognition. *Adv. Nutr.* **2012**, *3*, 465S–472S. [CrossRef]
39. Wang, B.; McVeagh, P.; Petocz, P.; Brand-Miller, J. Brain ganglioside and glycoprotein sialic acid in breastfed compared with formula-fed infants. *Am. J. Clin. Nutr.* **2003**, *78*, 1024–1029. [CrossRef] [PubMed]
40. Obelitz-Ryom, K.; Bering, S.B.; Overgaard, S.H.; Eskildsen, S.F.; Ringgaard, S.; Olesen, J.L.; Skovgaard, K.; Pankratova, S.; Wang, B.; Brunse, A.; et al. Bovine Milk Oligosaccharides with Sialyllactose Improves Cognition in Preterm Pigs. *Nutrients* **2019**, *11*, 1335. [CrossRef] [PubMed]
41. Dror, D.K.; Allen, L.H. Overview of Nutrients in Human Milk. *Adv. Nutr.* **2018**, *9*, 278S–294S. [CrossRef] [PubMed]
42. Krebs, N.F.; Lozoff, B.; Georgieff, M.K. Neurodevelopment: The Impact of Nutrition and Inflammation During Infancy in Low-Resource Settings. *Pediatrics* **2017**, *139*, S50–S58. [CrossRef] [PubMed]
43. Zeisel, S.H. The fetal origins of memory: The role of dietary choline in optimal brain development. *J. Pediatr.* **2006**, *149*, S131–S136. [CrossRef] [PubMed]
44. Tonjes, R.; Hecht, K.; Brautzsch, M.; Lucius, R.; Dorner, G. Behavioural changes in adult rats produced by early postnatal maternal deprivation and treatment with choline chloride. *Exp. Clin. Endocrinol.* **1986**, *88*, 151–157. [CrossRef]
45. Skeaff, S.A. Iodine deficiency in pregnancy: The effect on neurodevelopment in the child. *Nutrients* **2011**, *3*, 265–273. [CrossRef]
46. Ooylan, L.M.; Hart, S.; Porter, K.B.; Driskell, J.A. Vitamin B-6 content of breast milk and neonatal behavioral functioning. *J. Am. Diet. Assoc.* **2002**, *102*, 1433–1438. [CrossRef]
47. Copp, K.; DeFranco, E.A.; Kleiman, J.; Rogers, L.K.; Morrow, A.L.; Valentine, C.J. Nutrition Support Team Guide to Maternal Diet for the Human-Milk-Fed Infant. *Nutr. Clin. Pract.* **2018**, *33*, 687–693. [CrossRef]
48. Sabatier, M.; Garcia-Rodenas, C.L.; Castro, C.A.; Kastenmayer, P.; Vigo, M.; Dubascoux, S.; Andrey, D.; Nicolas, M.; Payot, J.R.; Bordier, V.; et al. Longitudinal Changes of Mineral Concentrations in Preterm and Term Human Milk from Lactating Swiss Women. *Nutrients* **2019**, *11*, 1855. [CrossRef]
49. Ejezie, F.; Nwagha, U.; Ikekpeazu, E.; Ozoemena, O.; Onwusi, E. Assessment of iron content of breast milk in preterm and term mothers in enugu urban. *Ann. Med. Health Sci. Res.* **2011**, *1*, 85–90. [PubMed]
50. Lemons, J.A.; Moye, L.; Hall, D.; Simmons, M. Differences in the composition of preterm and term human milk during early lactation. *Pediatr. Res.* **1982**, *16*, 113–117. [CrossRef] [PubMed]
51. Ford, J.E.; Zechalko, A.; Murphy, J.; Brooke, O.G. Comparison of the B vitamin composition of milk from mothers of preterm and term babies. *Arch. Dis. Child.* **1983**, *58*, 367–372. [CrossRef]
52. Atinmo, T.; Omololu, A. Trace element content of breastmilk from mothers of preterm infants in Nigeria. *Early Hum. Dev.* **1982**, *6*, 309–313. [CrossRef]
53. Maas, C.; Franz, A.R.; Shunova, A.; Mathes, M.; Bleeker, C.; Poets, C.F.; Schleicher, E.; Bernhard, W. Choline and polyunsaturated fatty acids in preterm infants' maternal milk. *Eur. J. Nutr.* **2017**, *56*, 1733–1742. [CrossRef] [PubMed]
54. Shunova, A.; Bockmann, K.A.; Minarski, M.; Franz, A.R.; Wiechers, C.; Poets, C.F.; Bernhard, W. Choline Content of Term and Preterm Infant Formulae Compared to Expressed Breast Milk-How Do We Justify the Discrepancies? *Nutrients* **2020**, *12*, 3815. [CrossRef] [PubMed]
55. Hsu, Y.C.; Chen, C.H.; Lin, M.C.; Tsai, C.R.; Liang, J.T.; Wang, T.M. Changes in preterm breast milk nutrient content in the first month. *Pediatr. Neonatol.* **2014**, *55*, 449–454. [CrossRef] [PubMed]
56. Daniels, L.; Gibson, R.S.; Diana, A.; Haszard, J.J.; Rahmannia, S.; Luftimas, D.E.; Hampel, D.; Shahab-Ferdows, S.; Reid, M.; Melo, L.; et al. Micronutrient intakes of lactating mothers and their association with breast milk concentrations and micronutrient adequacy of exclusively breastfed Indonesian infants. *Am. J. Clin. Nutr.* **2019**, *110*, 391–400. [CrossRef]
57. Moran, J.R.; Vaughan, R.; Stroop, S.; Coy, S.; Johnston, H.; Greene, H.L. Concentrations and total daily output of micronutrients in breast milk of mothers delivering preterm: A longitudinal study. *J. Pediatr. Gastroenterol. Nutr.* **1983**, *2*, 629–634. [CrossRef]

58. Lindeman, J.H.; van Zoeren-Grobben, D.; Schrijver, J.; Speek, A.J.; Poorthuis, B.J.; Berger, H.M. The total free radical trapping ability of cord blood plasma in preterm and term babies. *Pediatr. Res.* **1989**, *26*, 20–24. [CrossRef]
59. Selleg, I.; King, C.G. The Vitamin C Content of Human Milk and Its Variation with Diet. *J. Nutr.* **1936**, *11*, 599–606. [CrossRef]
60. Zheng, M.-C.; Yamaoka, K.; Okada, S.; Tanaka, Y.; Nishimura, K.; Wakimoto, H.; Seino, Y. Vitamin D metabolites in human milk from mothers of preterm and full-term infants. *J. Bone Miner. Metab.* **1990**, *8*, 11–16. [CrossRef]
61. Cormack, B.E.; Harding, J.E.; Miller, S.P.; Bloomfield, F.H. The Influence of Early Nutrition on Brain Growth and Neurodevelopment in Extremely Preterm Babies: A Narrative Review. *Nutrients* **2019**, *11*, 2029. [CrossRef]
62. Radmacher, P.G.; Adamkin, D.H. Fortification of human milk for preterm infants. *Semin. Fetal Neonatal Med.* **2017**, *22*, 30–35. [CrossRef] [PubMed]
63. Deoni, S.C.; Dean, D.C., 3rd; Piryatinsky, I.; O'Muircheartaigh, J.; Waskiewicz, N.; Lehman, K.; Han, M.; Dirks, H. Breastfeeding and early white matter development: A cross-sectional study. *Neuroimage* **2013**, *82*, 77–86. [CrossRef] [PubMed]
64. van Dyck, L.I.; Morrow, E.M. Genetic control of postnatal human brain growth. *Curr. Opin. Neurol.* **2017**, *30*, 114–124. [CrossRef]
65. Deoni, S.C.; Mercure, E.; Blasi, A.; Gasston, D.; Thomson, A.; Johnson, M.; Williams, S.C.; Murphy, D.G. Mapping infant brain myelination with magnetic resonance imaging. *J. Neurosci.* **2011**, *31*, 784–791. [CrossRef] [PubMed]
66. Poitelon, Y.; Kopec, A.M.; Belin, S. Myelin Fat Facts: An Overview of Lipids and Fatty Acid Metabolism. *Cells* **2020**, *9*, 812. [CrossRef] [PubMed]
67. Aggarwal, S.; Yurlova, L.; Simons, M. Central nervous system myelin: Structure, synthesis and assembly. *Trends Cell Biol.* **2011**, *21*, 585–593. [CrossRef]
68. Dimas, P.; Montani, L.; Pereira, J.A.; Moreno, D.; Trotzmuller, M.; Gerber, J.; Semenkovich, C.F.; Kofeler, H.C.; Suter, U. CNS myelination and remyelination depend on fatty acid synthesis by oligodendrocytes. *Elife* **2019**, *8*, e44702. [CrossRef]
69. Chang, C.Y.; Ke, D.S.; Chen, J.Y. Essential fatty acids and human brain. *Acta Neurol. Taiwan* **2009**, *18*, 231–241.
70. Blaas, N.; Schuurmann, C.; Bartke, N.; Stahl, B.; Humpf, H.U. Structural profiling and quantification of sphingomyelin in human breast milk by HPLC-MS/MS. *J. Agric. Food Chem.* **2011**, *59*, 6018–6024. [CrossRef]
71. Oshida, K.; Shimizu, T.; Takase, M.; Tamura, Y.; Shimizu, T.; Yamashiro, Y. Effects of dietary sphingomyelin on central nervous system myelination in developing rats. *Pediatr. Res.* **2003**, *53*, 589–593. [CrossRef]
72. Jana, A.; Pahan, K. Sphingolipids in multiple sclerosis. *Neuromolecular Med.* **2010**, *12*, 351–361. [CrossRef]
73. Saher, G.; Brugger, B.; Lappe-Siefke, C.; Mobius, W.; Tozawa, R.; Wehr, M.C.; Wieland, F.; Ishibashi, S.; Nave, K.A. High cholesterol level is essential for myelin membrane growth. *Nat. Neurosci.* **2005**, *8*, 468–475. [CrossRef]
74. Mizuta, H.; Amino, N.; Ichihara, K.; Harada, T.; Nose, O.; Tanizawa, O.; Miyai, K. Thyroid hormones in human milk and their influence on thyroid function of breast-fed babies. *Pediatr. Res.* **1983**, *17*, 468–471. [CrossRef]
75. Bernal, J. Thyroid hormones and brain development. *Vitam. Horm.* **2005**, *71*, 95–122. [CrossRef] [PubMed]
76. Isaacs, E.B.; Fischl, B.R.; Quinn, B.T.; Chong, W.K.; Gadian, D.G.; Lucas, A. Impact of breast milk on intelligence quotient, brain size, and white matter development. *Pediatr. Res.* **2010**, *67*, 357–362. [CrossRef]
77. Coviello, C.; Keunen, K.; Kersbergen, K.J.; Groenendaal, F.; Leemans, A.; Peels, B.; Isgum, I.; Viergever, M.A.; de Vries, L.S.; Buonocore, G.; et al. Effects of early nutrition and growth on brain volumes, white matter microstructure, and neurodevelopmental outcome in preterm newborns. *Pediatr Res.* **2018**, *83*, 102–110. [CrossRef] [PubMed]
78. Miller, J.B.; McVeagh, P. Human milk oligosaccharides: 130 reasons to breast-feed. *Br. J. Nutr.* **1999**, *82*, 333–335. [CrossRef] [PubMed]
79. Deoni, S.; Dean, D., 3rd; Joelson, S.; O'Regan, J.; Schneider, N. Early nutrition influences developmental myelination and cognition in infants and young children. *Neuroimage* **2018**, *178*, 649–659. [CrossRef] [PubMed]
80. Schneider, N.; Hauser, J.; Oliveira, M.; Cazaubon, E.; Mottaz, S.C.; O'Neill, B.V.; Steiner, P.; Deoni, S.C.L. Sphingomyelin in Brain and Cognitive Development: Preliminary Data. *eNeuro* **2019**, *6*. [CrossRef]
81. Melnik, B.C.; Schmitz, G. Milk's Role as an Epigenetic Regulator in Health and Disease. *Diseases* **2017**, *5*, 12. [CrossRef] [PubMed]
82. Verduci, E.; Banderali, G.; Barberi, S.; Radaelli, G.; Lops, A.; Betti, F.; Riva, E.; Giovannini, M. Epigenetic effects of human breast milk. *Nutrients* **2014**, *6*, 1711–1724. [CrossRef]
83. Moody, L.; Chen, H.; Pan, Y.X. Early-Life Nutritional Programming of Cognition-The Fundamental Role of Epigenetic Mechanisms in Mediating the Relation between Early-Life Environment and Learning and Memory Process. *Adv. Nutr.* **2017**, *8*, 337–350. [CrossRef]
84. Naninck, E.F.; Lucassen, P.J.; Korosi, A. Consequences of early-life experiences on cognition and emotion: A role for nutrition and epigenetic mechanisms. In *Oxford Handbook of Molecular Psychology*; OUP: Oxford, UK, 2015. [CrossRef]
85. Benmoussa, A.; Laugier, J.; Beauparlant, C.J.; Lambert, M.; Droit, A.; Provost, P. Complexity of the microRNA transcriptome of cow milk and milk-derived extracellular vesicles isolated via differential ultracentrifugation. *J. Dairy Sci.* **2020**, *103*, 16–29. [CrossRef] [PubMed]
86. Janas, A.M.; Sapon, K.; Janas, T.; Stowell, M.H.; Janas, T. Exosomes and other extracellular vesicles in neural cells and neurodegenerative diseases. *Biochim. Biophys. Acta* **2016**, *1858*, 1139–1151. [CrossRef] [PubMed]
87. Floris, I.; Kraft, J.D.; Altosaar, I. Roles of MicroRNA across Prenatal and Postnatal Periods. *Int. J. Mol. Sci.* **2016**, *17*, 1994. [CrossRef] [PubMed]

88. Moncini, S.; Lunghi, M.; Valmadre, A.; Grasso, M.; Del Vescovo, V.; Riva, P.; Denti, M.A.; Venturin, M. The miR-15/107 Family of microRNA Genes Regulates CDK5R1/p35 with Implications for Alzheimer's Disease Pathogenesis. *Mol. Neurobiol.* **2017**, *54*, 4329–4342. [CrossRef] [PubMed]
89. Munch, E.M.; Harris, R.A.; Mohammad, M.; Benham, A.L.; Pejerrey, S.M.; Showalter, L.; Hu, M.; Shope, C.D.; Maningat, P.D.; Gunaratne, P.H.; et al. Transcriptome profiling of microRNA by Next-Gen deep sequencing reveals known and novel miRNA species in the lipid fraction of human breast milk. *PLoS ONE* **2013**, *8*, e50564. [CrossRef] [PubMed]
90. Quitadamo, P.A.; Palumbo, G.; Cianti, L.; Lurdo, P.; Gentile, M.A.; Villani, A. The Revolution of Breast Milk: The Multiple Role of Human Milk Banking between Evidence and Experience-A Narrative Review. *Int. J. Pediatr.* **2021**, *2021*, 6682516. [CrossRef] [PubMed]
91. Cregan, M.D.; Fan, Y.; Appelbee, A.; Brown, M.L.; Klopcic, B.; Koppen, J.; Mitoulas, L.R.; Piper, K.M.; Choolani, M.A.; Chong, Y.S.; et al. Identification of nestin-positive putative mammary stem cells in human breastmilk. *Cell Tissue Res.* **2007**, *329*, 129–136. [CrossRef]
92. Molinari, C.E.; Casadio, Y.S.; Hartmann, B.T.; Livk, A.; Bringans, S.; Arthur, P.G.; Hartmann, P.E. Proteome mapping of human skim milk proteins in term and preterm milk. *J. Proteome Res.* **2012**, *11*, 1696–1714. [CrossRef]
93. Fitzstevens, J.L.; Smith, K.C.; Hagadorn, J.I.; Caimano, M.J.; Matson, A.P.; Brownell, E.A. Systematic Review of the Human Milk Microbiota. *Nutr. Clin. Pract.* **2017**, *32*, 354–364. [CrossRef] [PubMed]
94. Bardanzellu, F.; Peroni, D.G.; Fanos, V. Human Breast Milk: Bioactive Components, from Stem Cells to Health Outcomes. *Curr. Nutr. Rep.* **2020**, *9*, 1–13. [CrossRef] [PubMed]
95. Pacheco, A.R.; Barile, D.; Underwood, M.A.; Mills, D.A. The impact of the milk glycobiome on the neonate gut microbiota. *Annu. Rev. Anim. Biosci.* **2015**, *3*, 419–445. [CrossRef] [PubMed]