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Integrative perspective on the maternal Gut-Brain-Breast axis: Linking dietary polyphenols, mental health, and human milk composition

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Highlights

- **During reproductive stages, women undergo changes in cognitive functioning**
- **Exposure to dietary phytochemicals plays a key role in regulating cognitive functions**
- **Human milk is a dynamic biological fluid influenced by mental health and diet**
- **Microbiota regulates neural pathways controlling cognition and human milk.**
- **Polyphenols are the main phytochemicals with promising effects on women's health**

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Integrative perspective on the maternal Gut-Brain-Breast axis: Linking dietary polyphenols, mental health, and human milk composition

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Abstract

This narrative review examines the interplay between maternal diet (particularly polyphenol intake), cognition, and human milk composition during the postpartum period. Early motherhood involves substantial neurobiological and psychological adaptations that, together with stress, sleep disturbances, and other mental health challenges, can influence maternal cognition and lactation physiology. Emerging evidence indicates that dietary polyphenols interact with the gut microbiota to produce bioactive metabolites capable of modulating neuroinflammatory pathways, neurotransmission, and endocrine signaling relevant to maternal cognitive function. Maternal polyphenol consumption may also contribute to variations in human milk composition, including antioxidant activity and lipid profile, which can influence both maternal and infant health outcomes.These complex interactions can be conceptualized through a gut-brain-breast axis framework, highlighting how nutritional, psychological, and microbial factors converge to support postpartum well-being. While most current evidence is derived from preclinical studies, these findings emphasize the potential of integrative perinatal strategies that combine diet, mental health support, and microbiota-targeted interventions to optimize maternal and infant outcomes. Future research should focus on controlled human studies to clarify underlying mechanisms and effects, providing evidence for nutritional strategies that strengthen the gut-brain-breast axis in support of maternal mental health.

Keywords: Postpartum Period; Cognition; Diet; Polyphenols; Microbiota; Lactation.

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1. Introduction

Supporting postpartum well-being requires a holistic approach by the health system, which must be addressed before birth [1]. Traditionally, postpartum medical care has been focused on physical aspects related to the involution of reproductive organs and newborn care [2]. Nonetheless, it is essential that health services recognize puerperium as a stage with physiological, emotional, and social changes, significantly impacting women's everyday life. Concerning this, maternal care should adopt a health rights perspective that takes into account individual experiences and subjectivities [3]. Given the complexity of these health issues, an integrative approach of the state of the art is necessary. Thus, a narrative review was carried out following the Scale for the Assessment of Narrative Review Articles [4], including studies with the aim of revising the complex interplay between maternal cognitive status, polyphenols intake, and human milk composition in women during puerperium. This review offers a novel and integrative perspective on postpartum health by connecting three physiological systems traditionally studied in isolation (gut, brain, and mammary gland) through the modulatory role of dietary polyphenols (Figure 1).

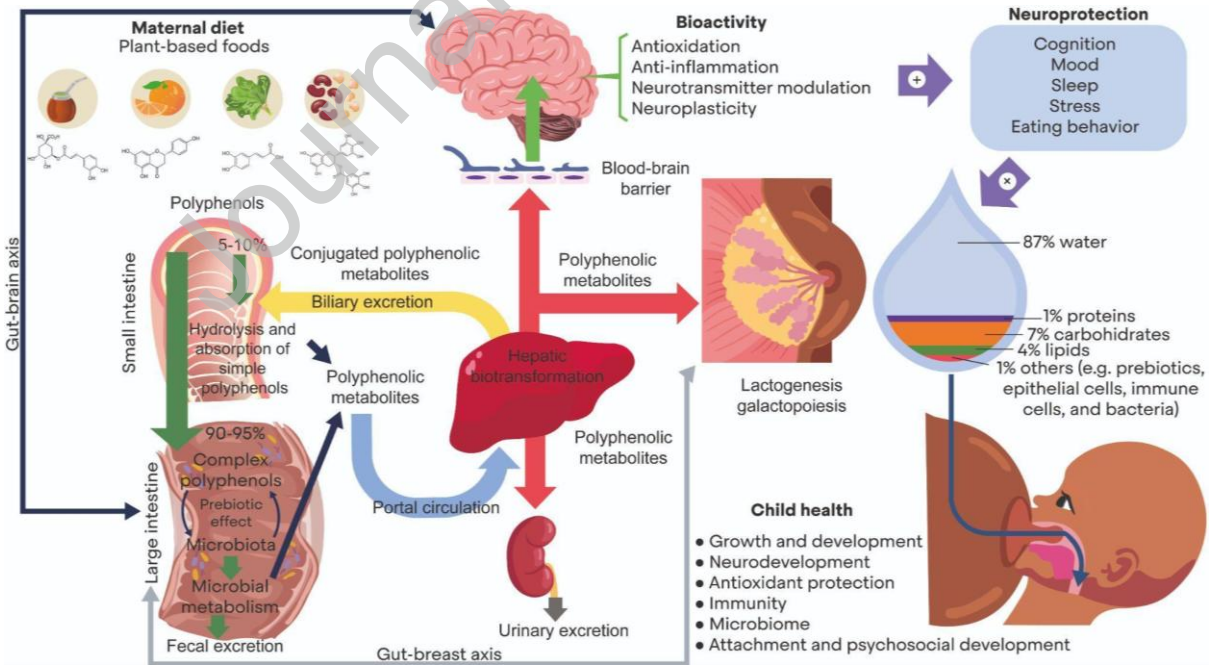


Figure 1. Interplay between the gut, brain, and mammary gland mediated by dietary polyphenols.

Primarily, the review focuses on neurophysiological changes driven by hormonal fluctuations during reproductive stages. Furthermore, cognitive variations and complaints, and their impacts related to insomnia and stress are examined. Secondly, the neuromodulating roles of diet and microbiota are addressed, particularly regarding how polyphenol intake may influence maternal cognition and mental well-being. Finally, the review explores how cognition and diet may condition human lactation and milk composition.

This work proposes an emerging framework for the gut-brain-breast axis. By integrating neurocognitive changes, diet-microbiota interactions, and lactation physiology, it advances a holistic understanding of maternal adaptation during the puerperium and offers novel translational opportunities for comprehensive perinatal health strategies. We hypothesize that, during the postpartum period, dietary polyphenol intake modulates maternal mental health and lactation physiology through multiple interconnected pathways, including direct effects on the brain and mammary gland, gut microbiota-mediated mechanisms, neuroendocrine regulation, and reciprocal interactions among these systems, ultimately influencing human milk composition. Specifically, polyphenols are proposed to act upstream in a gut-brain-breast axis, whereby polyphenol-microbiota interactions generate bioactive metabolites that support maternal well-being and shape the quantity and quality of bioactive components in human milk.

2.1 Neurophysiological changes and mental health challenges associated with motherhood

Pregnancy and postpartum constitute a dynamic period involving hormone-driven neurophysiological changes, which include processes of neuroplasticity [5]. Research has consistently demonstrated structural modifications in the maternal brain, such as alterations in the volume of various brain regions (including reductions in gray matter) and ventricles, as well as evidence of neural restoration or rejuvenation [6-9]. While some of these structural changes are transitory, others may persist throughout life and even act as protective factors,

underscoring their importance for the development of maternal behavior and the long-term aspects related to motherhood [10, 11]. These neurobiological changes, coupled with additional factors such as the social environment and individual genetics, exert an influence on overall cognitive functioning [12, 13]. The transition to motherhood involves a complex cognitive reorganization, characterized by a coexistence of specific functional improvements and declines in essential cognitive domains [10, 14, 15].

Several studies have reported heterogeneous findings regarding cognition during the postpartum period, with some studies reporting negative effects [16-19], others showing no significant changes [20, 21], and some even suggesting potential cognitive benefits [22-27] (Figure 2). On the one hand, some evidence indicates that the cognitive processing of infant-related stimuli may be selectively enhanced during this stage, manifesting as greater speed and accuracy in face recognition and functional changes in auditory capacities [28, 29]. These modifications are thought to represent a psychological preparation for motherhood and may serve as powerful predictors of the strength of the early maternal bond [30, 31]. Crucially, these specialized processes are dependent on the mother's mood state [32]. Conversely, postpartum women tend to exhibit lower scores when assessed with traditional cognitive tests that evaluate generalized domains such as attention, memory, visuospatial abilities, and processing speed, among others [33-37]. Furthermore, parity has also been identified as a potential moderating factor, with studies showing that multiparous postpartum women perform better on verbal fluency tests than their primiparous counterparts [38]. Multiparity may contribute to cognitive adaptation through reorganization processes associated with reproductive experience [12]. According to Pereira and Ferreira [39], cognitive functions facilitate the perception and interpretation of offspring cues to meet their needs. Although some neuroimaging studies suggest that reproductive history is associated with structural changes in white (e.g., corpus callosum) and gray matter (e.g., cortical thickness) that could underlie

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cognitive adaptations [11, 36], the evidence remains limited and primarily correlational. The aggregated impact of these variations, both positive and negative, on the daily life and adaptive capacity of the mother can be significant and durable [22, 40].

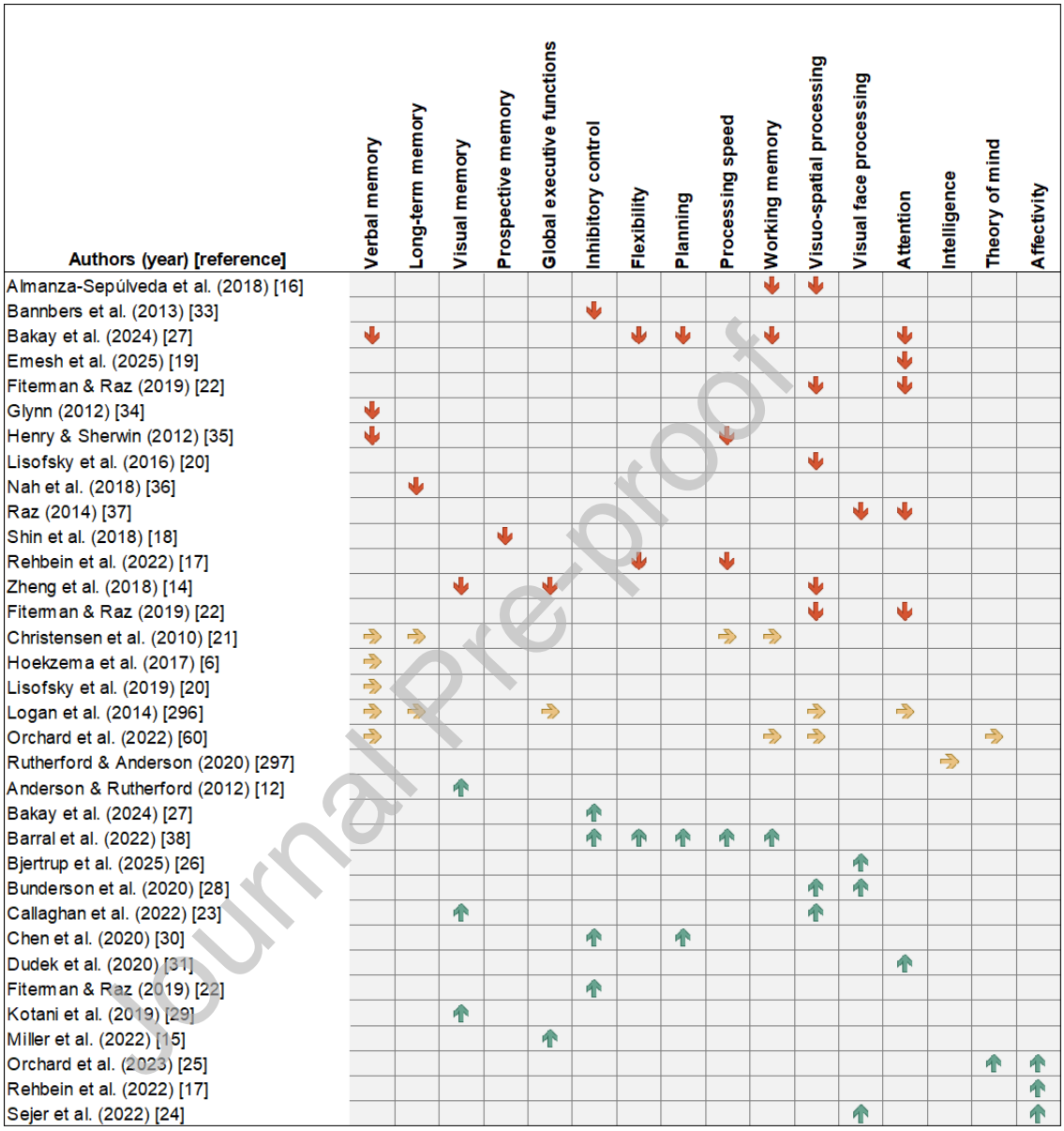


Figure 2. Results of studies on the effects of peripartum on cognitive functioning. Red arrows = decrease, yellow arrows = no change, green arrows = increase.

Regarding postpartum mental health, sleep disturbances (particularly insomnia) are commonly reported among women during this period. Poor sleep quality is specifically linked to sleep fragmentation in lactating women [41], although difficulty falling asleep and early

awakenings are also frequently described [42, 43]. These sleep alterations and resulting sleep deprivation may significantly compromise diurnal functioning [44, 45]. Moreover, insomnia has been linked to an increased risk of co-occurring conditions such as depression, anxiety, fatigue, familial dysfunction, and an impaired infant bond [46, 47]. In addition to sleep disturbances, moderate levels of psychological stress are prevalent among postpartum women [48, 49]. The postpartum period is recognized as a stage of heightened vulnerability to stress due to the new challenges and biopsychosocial changes linked to motherhood [50]. Moreover, the severity of symptoms is often amplified by social and environmental stressors, such as socioeconomic factors (e.g., living in low-income settings and inadequate access to healthcare). Importantly, psychological stress and insomnia are reciprocally reinforcing, creating a vicious cycle that further compromises maternal well-being. [51, 52].

The mode of delivery plays a crucial role in shaping women's physical and mental health [53]. Some studies suggest that vaginal delivery is associated with more favorable maternal cognitive outcomes, whereas cesarean section, particularly emergency procedures, may be linked to poorer psychological adjustment [54]. In this context, Cesarean section has been associated with changes in postoperative mood, self-esteem, stress, and cognitive dysfunction [55]. This topic has increasing relevance, as the global rate of cesarean deliveries has more than doubled in the past 15 years [56], exceeding the World Health Organization's recommended threshold of 10-15% [57]. Some countries report especially high rates; for instance, in Argentina, cesarean deliveries account for approximately 35% of births in the public sector and 70% in the private sector [58]. Current evidence recommends combining cognitive and physical training with diet optimization, both before and after delivery, to improve postpartum quality of life [59].

It is important to emphasize that women with lower mental well-being during the postpartum period (i.e., experiencing greater anxiety, insomnia, stress, and depressive

symptoms) tend to report greater subjective cognitive complaints, which have been consistently associated with the severity of insomnia and perceived stress [60, 61]. The term subjective cognitive complaints refers to a broad range of self-perceived cognitive difficulties across memory, language, attention, and executive domains [62]. In postpartum women, subjective cognitive complaints are heterogeneous and variably reported [63, 64], with prevalence estimates ranging considerably from as low as 2% to as high as 82% [65]. The most frequently affected domains are executive functions (i.e., higher-order cognitive processes for planning, focusing, and regulating behavior) and memory, which include distraction, inflexibility, forgetfulness and the tip-of-the-tongue phenomenon. The commonly reported tip-of-the-tongue phenomenon (i.e., a temporary inability to retrieve a known word from memory, accompanied by a strong sense of imminent recall) could be interpreted as evidence that metacognitive and psycholinguistic processes may be particularly sensitive to changes occurring during the puerperium [66, 67]. Notably, a characteristic feature of this period is the discrepancy often observed between subjective complaints and objective cognitive performance. In this sense, subjective concerns about fronto-executive and memory functioning are not always associated with a corresponding lower performance in objective neuropsychological tests [68]. Furthermore, this incongruence may also respond to a higher self-awareness during this period, leading to frequent (re)testing of subjective memory [60].

2.2 Polyphenols consumption and the neuromodulatory role of diet during motherhood

Few studies have explored how dietary choices influence cognitive health in women transitioning to motherhood, a stage marked by heightened nutritional needs [69]. Such knowledge is crucial for identifying and addressing dietary needs and for supporting maternal biopsychosocial health [70-72]. The maternal brain undergoes the aforementioned changes that impact mental health. This issue may be modulated by different strategies that reduce negative changes but promote the positive ones. In this sense, promoting nutritional health is key for

enhancing the gut-brain-breast axis, with some dietary patterns being neuroprotective. They mainly include plant foods that show protective effects attributed to various nutrients and antioxidant polyphenols, among other mechanisms [73]. These bioactive compounds counteract oxidative stress, which is a biochemical process proposed as an etiological factor of non-communicable diseases [74, 75]. Related neuroprotection acts on nervous centers involved in the systemic regulation of metabolic homeostasis, which improves physical and mental well-being [76].

The main dietary sources of polyphenols are fruits and vegetables, juices, tea, coffee, yerba mate, wine, cereals, and chocolate [77]. Postpartum women approximately intake one gram of dietary polyphenols per day. The most consumed families are phenolic acids (e.g., caffeoylquinic acids), followed by flavonoids (e.g., hesperetin) and lignans (e.g., lariciresinol), with scarce stilbenes (e.g., resveratrol) [78, 79]. This pattern likely reflects the specific dietary choices of breastfeeding women, who often avoid certain beverages containing stilbenes [80]. According to the systematic review of Del Bo et al. [77], polyphenol intake is influenced by a range of factors (including geography, individual characteristics, social determinants, and habitual dietary practices) leading to substantial variability across populations. As an example, the main source of hydroxycinnamic acids is coffee worldwide, whereas yerba mate (traditional tea of *Ilex paraguariensis*) is the main polyphenol-rich beverage consumed in South American countries [81, 82], particularly among postpartum women [79].

After intake, polyphenolic bioavailability and indirect mediators in the central nervous system trigger antioxidant, anti-inflammatory, antiproliferative, antiplatelet, anti-atherosclerotic, and antiangiogenic effects, among others [83]. Effects on cognition and mood are due to modulation of synaptic plasticity and neurotransmitter pathways [84]. In addition, polyphenols have been reported to promote increased cerebral blood flow, learning ability,

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memory, executive functions, sustained attention, alertness, and global cognition [85-90]. Moreover, polyphenols may exert integrative beneficial effects by promoting maternal mental health [91], human lactation [92], and well-being during pregnancy and postpartum [93]. Higher levels of polyphenol intake have been associated with a lower prevalence of insomnia, depression, and anxiety, as well as with a better quality of life [94-96]. Likewise, the modulatory effects of polyphenols are receiving increasing attention as a potential approach for the treatment of mood disorders triggered by stressful conditions, such as those occurring during pregnancy or the puerperium [97, 98].

A study conducted in healthy women in the United States demonstrated that the consumption of lignans was associated with better verbal memory [99], which corresponds to a functional improvement in the prefrontal cortex [100]. Research in animal models reports neuroprotective effects of lignans, which cross the blood-brain barrier to bioaccumulate in the hypothalamus and modulate memory through an enhancement of the cholinergic system [100-102]. In addition, some research suggests endocrine and redox bioactivity as possible mechanisms of lignans [103], as well as an interaction with gut microbiota that modulates the gut-brain axis [104]. As an example, oral administration of lignans in animal models has been linked to an increase in *Lactobacillus* and *Bifidobacterium* [105], which are known to promote cognitive activity [106]. These bacteria also produce neuroactive mediators that directly influence the brain by regulating neurotransmission [107].

The interaction of flavonoids with the nervous system is documented [108]. These compounds cross the blood-brain barrier and may exert a neuroprotective effect on brain architecture by strengthening blood flow and signaling pathways in areas related to learning and memory [109, 110]. Hesperetin and naringenin, as well as their metabolites, are lipophilic

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flavanones with a high capacity to cross blood-tissue barriers [109], to a greater extent than more polar flavonoids, such as anthocyanins, epicatechins, and their metabolites [111].

Preclinical research confirms that hesperetin has neuroprotective actions on the hippocampus through its capacity to increase reduced glutathione and antioxidant enzymatic activity with decreased lipid peroxidation [112]. In addition to this antioxidant effect, this polyphenol is suggested to trigger positive effects on synaptic plasticity through activation of the phosphoinositol 3-kinase pathway in cortical and hippocampal neurons [113]. Ishola et al. [114] found that oral administration of hesperetin improves cortico-hippocampal antioxidant defense and cholinergic and trophic signaling, which are related to improved learning and memory in a scopolamine-induced amnesia model in mice. Other authors report that hesperetin modulates neuroinflammatory and apoptotic pathways [115]. In addition, a citrus extract with 88.2% hesperidin and 6.5% naringin modifies intestinal microbiota composition [116]. This extract promotes Firmicutes (*Enterococcus* and *Roseburia*) and Bacteroidetes (*Bacteroides*), leading to changes in the production of short-chain fatty acids and neuropeptides. These microbial metabolites may modulate the gut-brain axis, neuroinflammation, blood-brain barrier permeability, neurotransmitter production, and inhibitory/excitatory balance in the frontal cortex [117].

Scarce human trials assess the cognitive effects of hesperetin, reporting associations with increased cerebral blood flow, memory performance, and cognition [118]. A randomized, controlled, double-blind clinical trial was conducted by Kean et al. [119] in healthy adults, who received a juice with 549 mg/L of hesperidin (glycosidic form of hesperetin) and 60 mg/L of narirutin (another flavanone), or a juice with 64 mg/L of hesperidin and 10 mg/L of narirutin. The first group showed improvements in global cognitive function, episodic memory, and executive function. Similarly, Lamport et al. [120] found that hesperidin was associated with positive effects on executive performance in another randomized, single-blind, placebo-

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controlled clinical study. Participants were healthy young adults who received 500 mL of beverage (a high-flavanone group and a no-flavanone control combined with an energizer and vitamin C). The authors concluded that these flavanones in amounts commonly consumed may rapidly enhance cerebral blood flow, specifically in the right frontal gyrus (an area involved in tasks that require inhibition, planning, decision-making, and other aspects of executive functioning).

There is less research focused on their effects on forgetting, with some information about long-term memory and forgetting mechanisms [121]. There is evidence that a low consumption of polyphenols is related to greater interferences and poorer memory [122]. Memory interference is a type of forgetting that occurs when there is competing additional information before, after, or during the encoding of target information [123]. The susceptibility to interference is greater if the competing information is similar, as is the case in the two-word lists that make up the Rey Auditory Verbal Learning (RAVLT) test [104, 124]. Lariciresinol, hesperetin, and caffeic acid have been associated with a reduction in proactive and retroactive interference, with the latter being also related to gallated flavanols [125]. Proactive interference occurs when previously acquired knowledge hinders the ability to acquire new information, while retroactive interference refers to the effect of new learning on recall of previously established knowledge, affecting memory consolidation [123]. Consequently, retroactive interference occurs more frequently and is more detrimental to memory [126]. There is limited evidence about the effect of polyphenols on interference phenomena. Some studies show that the intake of polyphenol-containing foods may improve memory consolidation through decreased interference [127-129], although other studies report non-significant results [130, 131], or inverse results [132]. However, hippocampal neurogenesis in adults may favor the reduction of memory interference [133], being a neuroplastic process responsive to diet that occurs in the brains of postpartum women [134]. In addition, a lower interference in polyphenol

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consumers may depend on other cognitive processes (such as executive and attentional functions) involved in memory interference attenuation mechanisms (i.e., pattern separation and differential activation) [123].

Hydroxycinnamic acids are highly consumed by postpartum women and have been associated with better cognitive functioning. Nonetheless, there is scarce evidence about the effects of chlorogenic acids in terms of human brain function [135]. Their neuroprotective and neuromodulator potential has been studied experimentally, but published data report mixed results. On the one hand, Cropley et al. [136] in a double-blind, placebo-controlled study, report improvements in mood, attention, and behavior in healthy older adults after the acute administration of decaffeinated coffee with chlorogenic acid. Conversely, Camfield et al. [137] conducted a randomized controlled trial in sixty healthy adults over 50 years of age who were administered 6 g of a blend of decaffeinated green coffee with 540 mg of chlorogenic acids or a placebo, without observing significant cognitive benefits. The cognitive effects of chlorogenic acids may be mediated by improvements in mood and activation of benzodiazepine receptors [138], anti-acetylcholinesterase effects [139], and antioxidant mechanisms [140]. Also, dietary chlorogenic acid supplementation may act as a prebiotic that favors healthy neuroactive microbiota, which alleviate neuroinflammation and synaptic damage [141].

Ferulic and caffeic acids exhibit a stronger association with brain outcomes than chlorogenic acids [125]. These compounds have pharmacokinetic advantages, with a higher absorption than other polyphenols [135]. Caffeic acid modulates oxidative stress, 5-lipoxygenase activity, and neuronal death, which enhances learning and memory [136]. Ferulic acid also exerts these mechanisms and regulates neuroglia metabolism [137]. Moreover, these phenolic acids stimulate the production of short-chain fatty acids because of their prebiotic effects on the intestinal microbiota [142, 143].

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Catechin intake has also been associated with a better cognitive profile during postpartum [125]. Catechins are composed of simple catechin, epigallocatechin, epicatechin, gallocatechin, epigallocatechin gallate, and epicatechin gallate. They are classified into gallated and non-gallated types depending on the presence or absence of gallic moieties. Although both forms are bioactive, the main neurological benefits have been largely attributed to the gallated forms, given their different pharmacokinetics. In this sense, the non-gallated catechins are metabolized by phase II processes in the small intestine and liver to form conjugates in blood plasma and urine. The gallated forms remain mostly intact in the plasma to be excreted through the bile and metabolized by the colonic microbiota [144]. Epigallocatechin gallate has been reported to reduce anxiety and to increase activity in the anterior and medial frontal gyrus, with potential improvements in memory, social cognition, attention, and recall, among other cognitive functions [145-147]. Several biological mechanisms are responsible, such as antioxidant activity, iron chelation, improvement of parietal-frontal connectivity due to neuroplastic changes in N-methyl-D-aspartate (NMDA) receptors, interaction with γ-aminobutyric acid type A (GABAA) receptors [148], and anti-amyloidogenic activity [149]. In addition, catechins and their metabolites may regulate gut balance by modulating microbiota composition that favors the gut-brain axis [150, 151].

Beyond their biological effects, understanding how postpartum women access and adhere to polyphenol-rich diets is essential, as dietary patterns both determine intake levels and may influence health outcomes. Several studies have shown that sociodemographic factors, such as educational level, occupational status, and marital status, influence the nutritional status of postpartum women. For example, Pedersen et al. [152] reported that postpartum women with low income, unstable employment, and adverse psycho-emotional conditions were more likely to be at higher risk of weight retention and obesity. Similarly, insufficient physical activity and poor dietary habits have been associated with negative postpartum nutritional outcomes [153-

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155]. Although there is vast evidence that associates anthropometry with cognitive functioning in children, young adults, and older adults [156-158], this issue has been relatively underexplored in postpartum women. A high-fat diet has been associated with increased body weight and glucose intolerance in a postpartum mouse model, which was linked to behavioral changes, anxiety, cognitive dysfunction, and anhedonia [159]. An excessive body mass index and body adiposity during the peripartum may impair neuroplasticity [160]. For example, overweight and obesity during pregnancy have been shown to modify neurogenesis in the hippocampus, accompanied by memory deficits in postpartum women [161]. Furthermore, Xavier et al. reported that an obesogenic diet can alter the neuroimmune balance, affecting microglial activation and neurogenesis in the postpartum rat brain. In this sense, the maternal diet may influence the morphology, distribution, and function of hypothalamic microglia with changes in different brain regions, such as the basolateral amygdala and hippocampus [134].

Regarding behavior-related factors, individuals with a lower educational level are more likely to adopt dietary patterns characterized by a low intake of plant-based foods and a high intake of fats [162, 163]. The educational level is one of the most significant factors influencing food choices, as it shapes attitudes towards healthy eating, nutritional knowledge, social support, and family values [164]. Also, neuropsychological performance is mainly influenced by the type and level of education [165], functioning as a neuroprotector against cognitive deterioration [166]. Educational experiences promote the development of executive functions by increasing exposure to reading habits, problem solving, and abstract reasoning activities [167]. Thus, individuals with a higher educational level tend to show greater executive performance [166, 168]. Likewise, education improves the results of tests of language, memory, and executive functions [169, 170]. Consequently, education may act as a protective factor during the transition to motherhood by simultaneously promoting healthier dietary behaviors and enhancing cognitive resilience.

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In addition to diet, the role of the gut in the axis depends on the intestinal microbiota, which is a diverse and complex ecosystem that plays a key homeostatic role in human physiology, regulating metabolism, immunity, the absorption of dietary compounds, and neural functioning through its metabolites. Furthermore, the intestinal microbiota and dietary polyphenols must interact to exert their health benefits [107] Only approximately 10% of polyphenols are absorbed in the small intestine, leaving the remaining 90% to be transformed by the colonic microbiota through reactions like deglycosylation and demethylation [171]. The human intestinal microbiota is a diverse and complex ecosystem, composed of over a thousand microbial species, that fulfills a key homeostatic role in host physiology [172]. In healthy individuals, reactions such as deglycosylation, dehydroxylation, and demethylation metabolize polyphenols into small, low-molecular-weight fragments that are more absorbable and remain longer in the bloodstream [107, 173]. This reciprocal relationship demonstrates that dietary polyphenols act as prebiotics, modulating microbial composition and activity by limiting pathogen proliferation and promoting the growth of beneficial bacteria [107, 174]. As a result, regulating microbiota composition through polyphenol consumption has emerged as a novel therapeutic intervention aimed at promoting intestinal balance, or eubiosis [175]. This stability is essential, as the microbiota regulates metabolism, immunity, the absorption of dietary compounds, and nervous system function via the gut–brain axis; consequently, a state of dysbiosis can significantly impact overall health [107, 174]. The microbial composition exhibits high inter-individual variability, influenced by numerous endogenous (e.g., genetics, hormonal changes, gestation, human milk exposure) and exogenous factors (e.g., diet, stress, geographic region, level of pollution) [176]. Notably, recent evidence demonstrates that the maternal microbiota is distinctly influenced by the peripartum period [46] and the practice of human lactation [177].

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Nutritional health requires a multidimensional approach that allows understanding of individual adherence to certain food combinations forming dietary patterns and their determinants [178, 179]. Concerning this, a phytochemical pattern has been identified in postpartum lactating women, including low-starch vegetables and different types of fruits. It competes with two unhealthier patterns known as macronutritional (characterized by processed meats, legumes, snacks, cheeses, whole grains, snack foods, and sweets) and energetic (composed of starchy vegetables, refined cereals, sugary drinks, animal fats, and oils) [158]. Macronutritional pattern is similar to the Western pattern, which has been associated with lower cognitive performance [180], although it also includes neurotrophic foods (vegetable proteins) [181]. Energetic pattern is considered a risk factor for cognitive disorders, neurodegenerative pathologies [182], anxiety, stress, and depression [183, 184]. In contrast, the phytochemical pattern shares characteristics with a prudent pattern that may promote cognitive health [185]. A plant-based diet is therefore generally related to better executive and memory performance and to lower levels of depression, anxiety, and stress [183, 184, 186, 187].

In consequence, the neuroprotective potential of polyphenols depends on their dietary intake, microbiota involvement, and resulting bioavailability of these compounds, their metabolites, and other metabolic mediators triggered. These events converge in the gut and initiate complex phenomena upstream in the axis under the influence of social determinants of health and individual characteristics.

2.3 Human milk as a dynamic fluid shaped by maternal and environmental factors

The composition of human milk is conditioned by multiple biological, psychological, social, environmental, dietary, and reproductive factors [188-195]. Several studies show that postpartum stress, depression, insomnia, and anxiety may negatively influence it [196-198], whereas social support and self-efficacy have a positive impact [199, 200]. In this sense,

interventions that improve the mental well-being of lactating postpartum women have shown promising effects on milk composition and neonatal health [201, 202]. Furthermore, breastfeeding practice itself contributes to maternal psychological stability and sleep regulation through psychoneuroendocrine mechanisms involving oxytocin and prolactin, which strengthen mother-infant synchrony and support postpartum recovery [203, 204].

Regarding gut involvement, the dietary polyphenol exposure could provide additional benefits extended to the newborn, as bioactive compounds can be transferred to human milk [205]. This is important because newborns are highly susceptible to oxidative damage and the pathogenesis of multiple diseases [206, 207]. Several studies have shown that maternal consumption of polyphenols may improve the antioxidant potential of human milk [195; 208, 209], exerting better antioxidant properties than artificial milk [210]. In addition, milk polyphenols may modulate infant intestinal microbiota, which could improve the maturation of the immune system and potentially help prevent chronic diseases in adulthood [211].

2.4 Polyphenols and lactation

Diet is a key factor that significantly influences the composition of human milk [212, 213]. Polyphenols are proposed as bioactive compounds whose presence in human milk depends on maternal dietary intake. They may influence the nutritional composition of milk and be transferred to the infant, potentially exerting antioxidant, anti-inflammatory, and lipid-increasing effects [125, 195]. While this review emphasizes maternal benefits, infant outcomes are mentioned only in relation to compositional changes in human milk rather than direct effects of polyphenols on the newborn. A summary of the evidence linking maternal polyphenol intake with human milk production and composition is provided in Table 1.

Table 1. Associations between maternal polyphenol intake and human milk production and composition

Compound or food item	Effect	Proposed mechanism	Model design	Reference
Polyherbal formula (rich in polyphenols: flavonoids, isoflavones, phenolic acids)	↑ Milk production	Upregulation of LALBA and AQP genes at the mRNA level.	Animal	Mustofa et al., 2020 [214]
Moringa oleifera (rich in polyphenols)	↑ Proteins, lipids, carbohydrates, and vitamin A	Activation of macronutrient synthesis	Clinical trial	Puspasari et al., 2020 [216]
Procyanidins	↑ Lipids	Modulation of PPAR, adiponectin receptors, lipogenesis, and hepatic metabolism	Animal	Caimari et al., 2017 [220]
Quercetin	↑ Milk production, lipids, and carbohydrates	Phytoestrogenic effect stimulating prolactin expression and release from the pituitary gland, as well as induction of prolactin receptor expression in primary mammary epithelial cells. Expression of β-casein, stearoyl-CoA desaturase, fatty acid synthase, and α-lactalbumin in mammary gland tissue.	Animal	Lin et al., 2018 [242]
Lignans (lariciresinol, pinoresinol)	↑ Lipids	Modulation of lipogenic genes (SREBF, PPARγ, FASN, LPL, SCD, and ACACA).	Animal	Palin et al., 2014 [238]
Banana flower flour (*Musa x paradisiaca*)	↑ Milk production	Estrogenic and proliferative activity in secretory cells	Clinical trial	Nordin et al., 2020 [243]
Hemerocallis citrina Baroni extract (quercetin, kaempferol)	↑ Milk production and secretion	Promotional effect mediated by the prolactin signaling pathway in the mammary gland.	Animal	Zhong et al., 2021 [241]
Ellagic acid-rich walnuts	↑ Urolithins in human milk; maternal metabotype determines milk urolithin profile; potential influence on infant gut colonization by Gordonibacter	Maternal ellagitannins are metabolized by gut microbiota into urolithins, which are transferred to human milk; maternal urolithin metabotype influences milk profile; close maternal-infant contact favors infant Gordonibacter colonization; urolithins may act as postbiotics contributing to anti-inflammatory effects.	Clinical trial	Cortés-Martín et al., 2020 [247]
Polyscias scutellaria extract (flavonoids, terpenoids, phenolic acids, and lignan)	↑ Milk production and ejection	Modulation of prolactin and oxytocin.	Animal	Budiono et al., 2023 [248]

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Kenikir (*Cosmos caudatus*)	↑ Milk production	Enhances prolactin hormone secretion	Clinical trial	Sulistiyah et al., 2025 [249]
Olea europaea L. Polyphenols	↑ Mono and Polyunsaturated fatty acids, protein, and lactose ↓ Saturated fatty acids		Animal	Di Meo et al., 2023 [250]
Green Noodles based on long bean leaves (*Vigna sinensis L.*, Polyphenolic content = 384 mg/kg)	↑ Milk production	Enhances prolactin hormone secretion	Clinical trial	Nurhidayah et al., 2025 [251]
Hemerocallis citrina Baroni	↑ Milk production and quality	Sixty-seven overlapping target genes were identified between phenols and lactation-related targets. The extract may improve impaired lactation by regulating AKT1, CASP3, and the PI3K-AKT signaling pathway, which was confirmed by cell experiments showing enhanced mammary cell proliferation and milk component synthesis	In vitro/ In silico	Chen et al., 2025 [252]
Ginger-spiced millet-soya drink	↑ Milk production	Enhances prolactin hormone secretion	Clinical trial	Tahiru et al., 2025 [253]
Tannic acid and tea polyphenols	↑ Proteins	Modulation microbiota leading to improvement of nitrogen metabolism	Animal	Zhao et al., 2025 [254]
Hemerocallis citrina Baroni (flavonoids; hexamethylquercetin as the main active compound)	↑ Milk production, proteins, lactose and lipids	Regulation of key genes in the PI3K-Akt pathway; interaction with STAT5A, PIK3CA, IGF1R, TP53, CCND1, BCL2, INS, AR, and DLD	Animal and cellular (in vitro)	Chen et al., 2024 [255]

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Polyphenols have been suggested to act as galactagogues by up-regulating α-lactalbumin and aquaporin genes [214]. Moreover, the intake of isoflavones and other phenolic compounds has been associated with an increase in milk protein content in animal models [215]. Recently, an experimental study in lactating women showed that the consumption of *Moringa oleifera* leaf flours, a traditionally used Asian plant, was associated with increases in lipids, carbohydrates, and especially proteins [216]. Milk proteins are locally produced in the

mammary gland, although a minor part is also derived from maternal plasma, with the secretion-favoring mechanisms being unknown to date [217].

Regarding milk lipid content, the metabolic regulation by polyphenols may involve the modulation of adipokine production [218, 219]. As an example, procyanidin has been associated with an increase in circulating levels of non-esterified free fatty acids and total adiponectin in lactating mice [220]. These mice exhibited changes in gene expression related to lipid metabolism and adiponectin signaling in the mammary gland, including the upregulation of adiponectin receptors 1 and 2, oxidoreductin 1 of the endoplasmic reticulum, and lipogenic enzymes such as fatty acid synthase, glycerol-3-phosphate acyltransferase, and diacylglycerol-O-acyltransferase 1. These changes may promote increased lipid and protein synthesis in milk, enhancing its nutritional quality. Conversely, breast fat and hepatic gene expression (adiponectin receptor 2 and fatty acid translocase) were reported to be reduced, suggesting a redistribution of lipids from maternal stores to milk. In the ovaries, peroxisome proliferator-activated receptor alpha (PPAR-α) expression was increased while adiponectin receptor 2 was downregulated, indicating enhanced fatty acid metabolism to support maternal energy balance during lactation. Collectively, these changes suggest that the increase in serum adiponectin may result from reduced hepatic clearance, further contributing to the regulation of lipid milk composition. Consequently, the coordinated metabolic and genetic changes induced by polyphenols may render breast milk a unique metabolic entity that could directly influence infant nutrition [221].

Lipids are the main energetic component of human milk, accounting for 50% of the infant's energy intake. These nutrients are also important for the supply of essential fatty acids, fat-soluble vitamins, and other bioactive components [222]. Triacylglycerols represent up to 98% of lipids, which are formed in the endoplasmic reticulum from fatty acids obtained from the circulation (released from adipose tissue reserves and dietary fat) or are synthesized *de novo*

by mammary epithelia from glucose. Milk triacylglycerols are located within the nucleus of fat globules [221]. Numerous factors can influence the gene transcription of enzymes [223], which allow milk fat composition to be regulated by maternal genetics and environmental factors [221]. This may explain the high inter-individual and intra-individual variations of lipid content [224].

PPARs, very low-density lipoprotein receptors (VLDLR), and adiponectin are lipid-regulating molecular pathways. PPARs are members of a subfamily of nuclear receptors that promote lipogenic genes and modulate lipid homeostasis and inflammatory responses. Thus, they are essential for maintaining milk quality and protecting newborns [221]. Regarding the effects of polyphenols on PPARs in the lactating mammary gland, studies are null. Other research reports an induction of the expression of genes related to lipid metabolism, including the PPAR family, after the consumption of foods rich in polyphenols [225]. Moreover, a flavonoid extract administered to a murine model of lactating females was found to trigger PPAR gene expression in the ovary, but the mammary response remains unknown [220]. Therefore, a supplementation with polyphenols may improve the utilization of fatty acids by extramammary white adipose tissue. Mammary PPARγ controls most of the lipogenic genes, such as the enzyme fatty acid synthase (FASN), acetyl-CoA carboxylase alpha (ACACA), and glycerol-3-phosphate acyltransferase (GPAT) [226, 227]. Given that these pathways can be enhanced after supplementation with polyphenols [220], the PPAR family is possibly a mammary target. On the other hand, the intake of cocoa (rich in flavonoids: epicatechin and catechin) has been associated with induction of PPAR and fatty acid translocase (FAT/CD36) in white adipose tissue of mice under a hypercaloric diet, which suggests that these polyphenols favor energy homeostasis [228]. Furthermore, these pathways may contribute to the uptake of fatty acids by certain tissues, such as the lactating mammary gland [229]. This might partly

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explain the amount of triacylglycerols in the milk of women who intake these flavonoids to a higher extent.

Mammary cells obtain long-chain fatty acids from circulating non-esterified fatty acids and lipoproteins [230]. Briefly, VLDLR cooperates with lipoprotein lipase to hydrolyze triacylglycerols and release long-chain fatty acids, which freely enter and accumulate in the extracellular space. Subsequently, fatty acids are taken and activated by adding coenzyme A by FAT/CD36, fatty acid transporter, and acetyl-CoA synthetase. Fatty acids entering cells are activated or bound to fatty acid-binding proteins to be transported to metabolically active enzymes after passive diffusion (*or flip-flop*). Most acetic acid and little ketone bodies serve as precursors for *de novo* fatty acid synthesis in the cytosol by FASN and ACACA after activation by acyl-CoA synthase [231]. Evolutionarily, early human lactation depends on a marked up-regulation of genes associated with blood fatty acid uptake lipoprotein lipase (LPL), FAT/CD36, scavenger receptor class B type 1 (SCARB1), and VLDLR) and intracellular transport/channeling (acyl-CoA binding protein (ACBP/DBI) and fatty acid binding protein 3 (FABP3)) [232].

Dietary polyphenols can modulate lipid metabolism by acting on different processes, such as adipocyte differentiation, adipogenesis, clearance, fatty acid oxidation, and lipolysis, which supports their potential use in the treatment of metabolic diseases [233]. In this regard, polyphenols have been reported to reduce serum triacylglycerol concentrations, which could be related to an increase in the uptake and catabolism of lipoproteins in peripheral tissues [234]. As an example, supplementation with a procyanidin extract has been shown to reduce blood triacylglycerol levels by two mechanisms. Firstly, hepatic induction of β-oxidation of fatty acids may increase triacylglycerol catabolism. Secondly, increased lipoprotein lipase gene expression (a PPAR-mediated mechanism) could enhance clearance in peripheral tissues [235]. On the other hand, Feng et al. [236] found that (-)-epigallocatechin gallate, kaempferol, and

quercetin from Korean *Litsea* tea are involved in effects on cholesterol metabolism by regulating receptors for LDL and VLDL. Another polyphenolic compound that may improve lipid metabolism is ellagic acid through LDLR induction [237].

Palin et al. [238] found that the genes involved in *de novo* lipid synthesis in mammary tissue were up-regulated in a bovine model fed with flaxseed husk, which was associated with an increase in the transcription factors sterol regulatory element-binding factor (SREBF) and PPARγ. On the contrary, Bernard et al. [239] observed a decrease in *de novo* synthesis of goat milk lipids under supplementation with sunflower or linseed oil, by effects that appeared independent of ACACA and FASN gene expression. Therefore, these results suggest that the gene expression of these enzymes is not the only mechanism related to the secretion of milk fat. Other plant derivatives, such as lignans and phenolic acids, may promote milk lipid content [125, 240, 241]. In this regard, quercetin has been associated with increased expression of stearoyl-CoA desaturase and FASN in the mammary gland of postpartum mice, which may depend on its phytoestrogenic activity that stimulates expression of prolactin receptors, increasing tissue sensitivity to this crucial hormone [242]. Furthermore, quercetin was linked to an increase in breast gene expression of β-casein and α-lactalbumin. Also, postpartum women who poorly consumed quercetin tend to present a lower milk nutrient concentration [125]. Therefore, quercetin is proposed as a phytoestrogen that could promote mammary gland development and milk production by enhancing prolactin effects, being promising to treat hypogalactosis [238]. This is consistent with the findings of Nordin et al. [243] on the lactogenic properties of banana flower flour (*Musa x paradisiaca*), a food source of flavonoids and other polyphenols. Using a clinical trial design, it was found that the volume of expressed human milk after consuming banana flower flour biscuits is increased, showing a positive correlation with infant weight. According to the authors, the mechanisms involved may include estrogenic and proliferative activity as well as secretory stimulation in mammary gland cells.

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In this sense, these cells synthesize glycerol from glucose to cover the demand required for lipid synthesis during the secretory activation phase [244].

Proper functioning of the maternal gastrointestinal tract is considered necessary to achieve an adequate composition of human milk [245]. Consequently, the gut-breast axis is currently emerging as a particular physiological entity. Herein, maternal intestinal microbiota plays a key role in the extraction, synthesis, and absorption of many nutrients and metabolites destined for the composition of human milk [245, 246]. Thus, dietary manipulation of the gut microbiota through polyphenols and beneficial dietary patterns represents a potential strategy to promote and support a healthy microbial community in lactating women [172].

2.5 Integrating maternal cognition and lactation physiology

Although a considerable number of studies focus on the effects of mental health status on the initiation, duration, and exclusivity of human lactation, few have evaluated its relationship with milk composition [190]. Table 2 offers an overview of studies that have specifically explored these associations, highlighting their key findings.

Table 2. Summary of studies examining associations between maternal psychological state and human milk composition

Reference	Sample / Design	Maternal psychological measure(s)	Human milk component(s)	Main findings	Direction of association
Bozack et al., 2021 [256]	n=80; cohort	Lifetime stress and negative life events during pregnancy (Life Stressor Checklist and Crisis in Family Systems-Revised survey)	Extracellular vesicles microRNAs	Stress associated with altered detection/expression of multiple miRNAs; enriched fatty acid metabolism pathways	Stress: altered EV-miRNAs

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Cao et al., 2023 [257]	n=115; cross-sectional (30-120 days postpartum)	Edinburgh Postnatal Depression Scale	Docosahexaenoic acid (fatty acid profile)	Depression ↓ milk DHA	Depression: ↓ DHA
Fernández-Tuñas et al., 2023 [258]	n=45; cohort (very preterm)	Parental stress scale: NICU	Milk volume, microbiota	Stress ↓ milk volume, altered milk microbiota (↓*Firmicutes*, ↑*Proteobacteria*)	Stress: ↓ volume; altered microbiota
Holdsworth et al., 2025. [266]	n=51 dyads; cross-sectional (1-6 months postpartum; exclusively breastfeeding)	Parenting Stress Index	Human milk microbiome (HMM)	Maternal postpartum stress ↑ HMM beta diversity and ↓ HMM richness. Two stress subscales linked to differential IFM genera (↑*Erysipelotrichaceae* UCG-003, ↓*Eggerthella*). Postpartum stress is not associated with IFM diversity.	Stress: ↑ HMM beta diversity; ↓ HMM richness; altered milk microbiome.
Juncker et al., 2022 [259]	n=96; cohort (days 10-24 postpartum)	Perceived psychological stress; hair, saliva, milk cortisol	Total fatty acids, PUFA, ω-6	High stress ↓ total FA & PUFA	Stress: ↓ FAs
Juncker et al., 2023 [260]	n=97; cohort (day 10-24 postpartum)	Perceived psychological stress; hair, saliva, milk cortisol	Protein-bound & free amino acids	Stress ↑ protein-bound AAs; correlated with milk cortisol	Stress: ↑ protein-bound AAs, altered human milk amino acid composition
Juncker et al., 2025 [261]	n=92; cohort (days 10 & 24 postpartum)	Perceived psychological stress; hair, saliva, milk cortisol	Milk microbiome	High stress ↓ *Streptococcus*, *Gemella*, and *Veillonella*, ↑ Staphylococcus, Corynebacterium and Acinetobacter	Stress: altered microbiome
Kawano et al., 2015 [262]	n=81; cross-sectional (2 w postpartum)	Profile of Mood States, General Health Questionnaire, and State-Trait Anxiety Inventory scales	SIgA	SIgA negatively correlated with negative mood and anxiety	A negative maternal psychological state: ↓ SIgA
Miranda et al., 2022 [125]	n=75; cross-sectional	Perceived psychological stress, Insomnia, cognitive tests, dietary intake	Lipid profile (triacylglycerols, cholesterol, oxidation)	Higher executive/attentional and memory functioning ↑ milk triacylglycerols and ↓ lipid oxidation	Better cognitive status: ↑ lipid quantity and quality

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Riedy et al., 2024 [263]	n=926; cross-sectional	Edinburgh Postnatal Depression Scale, State-Trait Anxiety Inventory S-Scale, Perceived Stress Scale	19 Human milk oligosaccharides	Stress and depression associated with specific HMOs (e.g., lacto-N-fucopentaose III, lacto-N-hexaose)	Maternal depression and stress: altered HMO profile
Rosen-Carole et al., 2024 [264]	n=26; cohort (moderately preterm)	Parental stress scale: NICU	IgA, cortisol	Maternal stress ↓ HM cortisol at w1, ↑ HM IgA at w5	Early postpartum: stress ↓ HM cortisol; Later postpartum: stress ↑ IgA, ↑ cortisol; HM IgA protective (↓ illness).
Serim Demirgoren et al., 2017 [265]	n=150; cross-sectional (8-15 d postpartum)	Depression & anxiety scales	Sodium and potassium in milk	Depression and anxiety ↑ Na and Na/K ratio	Stress and depression: ↑ Na/K ratio
Shukri et al., 2019 [201]	RCT (n=64; relaxation vs. control)	Perceived Stress Scale, Beck Anxiety Inventory	Milk cortisol, milk intake	Relaxation ↓ stress & milk cortisol, ↑ milk intake, infant weight gain	Relaxation: ↓ cortisol
Tekgündüz et al., 2023 [267]	n=90; cross-sectional (day 7 postpartum)	Perceived Stress Scale	Milk cortisol	Stress positively correlated with cortisol; higher in preterm mothers	Stress: ↑ cortisol
Tomaszewska et al., 2025 [268]	n=103; cross-sectional	Adverse Childhood Experiences	microRNAs, fatty acids	High ACE ↑ miR-142-3p/5p & miR-223-3p; ↓ middle chain fatty acids	ACE: altered miRNAs, ↓ MCFAs
Vacaru et al., 2023 [269]	n=73; longitudinal (birth, 2-12 w postpartum)	Adverse childhood experiences (ACEs), attachment, support	Milk cortisol	ACEs possibly ↓ cortisol (minimal effect)	ACE: ↓ cortisol (trend)
Yang et al., 2025 [270]	n=41; cohort (42 d & 3 mo postpartum)	Sleep and depression questionnaires	α-lactalbumin, osteopontin, κ-casein, αs1-casein, β-casein, total protein	At 42 days: Sleep disorder ↓ α-lactalbumin, osteopontin, κ-casein; Depression ↓ αs1-casein, β-casein, casein. At 3 mo: Most early associations disappeared or reversed. Gut microbiome variation linked to protein alterations.	Sleep disorders/depression at early postpartum: ↓ proteins

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Ziomkiewicz et al., 2021a [200]	n=103; cross-sectional (5 mo postpartum)	State Anxiety Inventory, salivary cortisol, Berlin Social Support Scale	SIgA, IgM, IgG, Lactoferrin	Anxiety ↓ SIgA & LF; social support ↑ IgG	Anxiety: ↓ immune factors; Support: ↑ immune factors
Ziomkiewicz et al., 2021b [190]	n=146; cross-sectional	Recent Life Changes Questionnaire, cold pressor cortisol reactivity (salivary)	Energy, fat, protein, lactose, fatty acid profile	Psychosocial stress ↓ fat, energy, MCFA, LC-SFA	Psychosocial stress: ↓ fat

Better executive, attentional, and memory functioning in women has been associated with a more favorable milk lipid profile, including higher-quality triacylglycerols with reduced oxidation [125]. Although the scarcity of studies on the subject limits interpretations, psychoneuroimmunoendocrinological mechanisms are likely involved. For example, Ziomkiewicz et al. [190] found that the maternal stress response is associated with an altered composition of human milk, showing an increase in lipid content in the short term, but that it is reversed in the long term by the endocrine response to stress. Furthermore, it has been documented that chronic stress triggers lipid oxidation [271]. Mohd Shukri et al. [201] experimentally investigated the physiological and psychological dynamics of mother-infant signaling during breastfeeding. The study evaluated the effects of a maternal relaxation intervention on maternal psychological state, milk intake, milk cortisol levels, and infant behavior and growth. Their findings indicated that a maternal relaxation intervention improved maternal well-being and appeared to positively influence breastfeeding-related outcomes, supporting the notion that maternal psychological state is connected to lactation.

Regarding sleep, studies suggest that insomnia may influence lactation. There is an inverse association between the concentration of cholesterol in human milk and the severity of insomnia, with endogenous mechanisms being possibly involved. In this sense, this nutrient comes from plasma and *de novo* synthesis [232, 272], which is controlled by physiological

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mechanisms sensitive to insomnia [273-276]. Mood disorders are also associated with milk composition, such as a reduction in secretory immunoglobulin A [262] and in β-endorphin [277], and elevated sodium levels [278].

The mental health of lactating women is a key factor that conditions self-efficacy and difficulties for breastfeeding [279]. In addition, it favors bonding with the infant and well-being [280]. Nutrient transfer to human milk is essential for the growth and development of the newborn, which depends on a complex interplay between psychic, neural, endocrine, and immunological factors that modulate the mammary gland and maternal brain to support milk production [281]. It is necessary to recognize the mental factors that intervene during lactation in order to comprehensively address postpartum health and breastfeeding promotion.

During postpartum, the reduction in neurogenesis is a crucial adaptive mechanism for the acquisition of care behaviors, maternal learning, and emotional regulation [10, 282, 283]. Human lactation modulates this neuroadaptive phenomenon in women through stimulation of the hypothalamic-pituitary-adrenal axis, suppressing hippocampal neurogenesis [284]. Exclusive breastfeeding has been associated with a healthy nutritional status and better cognitive functioning [125, 285]. Furthermore, women who breastfeed tend to show better performance in neuropsychological tests after the age of 50 [286].

Polyphenols have been related to various molecular pathways of lipid metabolism that are common to the brain and the mammary gland [287, 288]. Therefore, differences in the milk content of triacylglycerols and cholesterol may reflect a complex internal response, which may also be accompanied by cognitive improvement. Likewise, maternal behavior and milk production share neuroendocrine mediators, which determine lactation physiology and cognition [289, 290]. Considering human lactation as a response of a gut-brain-breast axis promotes an integrative approach that can improve by changing modifiable determinants. This

is a major concern in health, as human milk is the best source of nutrients and bioactive compounds for newborns, ensuring proper growth, development, and psycho-emotional strengthening [291, 292]. Moreover, it has a positive impact on the health of the postpartum women throughout life. According to the World Health Organization, breastfeeding should be exclusive up to 6 months and mixed up to 2 years postpartum [293]. This represents one of the most effective public health strategies to improve child health and survival [294]. In this sense, people breastfed for longer periods have lower morbidity and mortality related to infectious and non-communicable diseases, as well as better cognitive development [295].

3. Conclusion

This review comprehensively addresses the role of dietary polyphenols in modulating the gut-brain-breast axis of postpartum women, emphasizing their potential to influence maternal cognition and milk composition through microbiome-dependent mechanisms. Current evidence suggests that polyphenols interact with intestinal microorganisms to generate bioactive metabolites capable of crossing biological barriers, modulating neuroinflammatory pathways, and influencing neurotransmission and endocrine signaling relevant to lactation and mental function.

The evidence reviewed in this article indicates that dietary polyphenols influence lactation through multiple, partially independent yet interconnected pathways. To facilitate interpretation, these mechanisms can be conceptually organized into three principal levels of action. First, direct effects on mammary tissue are supported primarily by in vivo and in vitro studies. Polyphenols and polyphenol-derived compounds have been shown to modulate mammary epithelial cell function by regulating gene expression related to milk synthesis, including α-lactalbumin, aquaporins, lipogenic enzymes, and transcription factors such as PPARs and SREBF. These effects may occur independently of higher brain regulation and

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suggest that the mammary gland itself is a direct biological target of certain polyphenols, consistent with molecular evidence reported for botanical galactagogues.

Second, central neuroendocrine pathways represent an indirect but biologically plausible route through which polyphenols may influence lactation. By modulating maternal mental health, stress responsiveness, sleep quality, and cognitive-emotional regulation, polyphenols may modify hormonal signaling involving prolactin, oxytocin, and cortisol, all of which play key roles in lactogenesis and milk ejection. These effects may arise from both microbiota-dependent metabolites and microbiota-independent polyphenol actions that reach central nervous system targets.

Third, gut microbiota-mediated mechanisms act upstream and in parallel by transforming dietary polyphenols into bioactive metabolites with enhanced bioavailability. These metabolites can influence systemic inflammation, redox balance, endocrine signaling, and metabolic regulation, thereby affecting both brain and mammary gland function. In addition, maternal gut microbiota may indirectly shape human milk composition through its contribution to nutrient absorption, metabolic partitioning, and immune modulation. Importantly, these pathways should not be viewed as isolated. Rather, they form a dynamic and reciprocal network. Depending on the specific polyphenol, dose, dietary context, maternal metabolic state, and microbiota profile, certain pathways may predominate, while others act synergistically.

Perturbations in any one of these domains can propagate across the others, creating complex feedback loops that may contribute to psychological distress in postpartum women. Conversely, a nutrient-rich diet, including polyphenols and other bioactive compounds, can support a healthy microbiota, enhance cognitive and emotional well-being, and optimize milk composition, creating a positive cycle that benefits both mother and infant. These underscore the critical importance of adopting a holistic perspective when evaluating maternal and infant

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health during this susceptible stage, as interventions in one domain can have potentially cascading effects across the entire lactation network.

Nevertheless, it is important to note that the majority of existing data originates from animal and *in vitro* models, and translational evidence in humans remains scarce. Future research should prioritize controlled clinical interventions that integrate microbiome profiling, metabolomic analyses, and cognitive assessments to clarify relationships and identify underlying mechanisms. Other topics to be addressed are dose-response relationships, interindividual variability in polyphenol metabolism, and potential confounding by dietary patterns and psychosocial factors.

Conceptually, the gut-brain-breast axis represents a multidirectional communication network within the maternal physiology, where dietary factors and microbial metabolites can jointly modulate neural and mammary functions. While this review has focused specifically on polyphenols, other classes of phytochemicals such as carotenoids, phytosterols, monoterpenes, and omega fatty acids may also play relevant roles in modulating the gut-brain-breast axis, and therefore warrant further investigation. Expanding this framework beyond polyphenols to other plant-derived bioactives will be critical to defining nutritional strategies that enhance maternal neuroplasticity, milk bioactivity, and overall perinatal health.

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CRediT Author Statement

ARM: Conceptualization, Methodology, Investigation, Data Curation, Formal Analysis, Writing – Original Draft. **PEB:** Methodology, Investigation, Data Curation, Formal Analysis, Writing – Review & Editing. **SVS:** Supervision, Writing – Review & Editing. **EAS:** Conceptualization, Methodology, Supervision, Project Administration, Funding Acquisition, Writing – Review & Editing.

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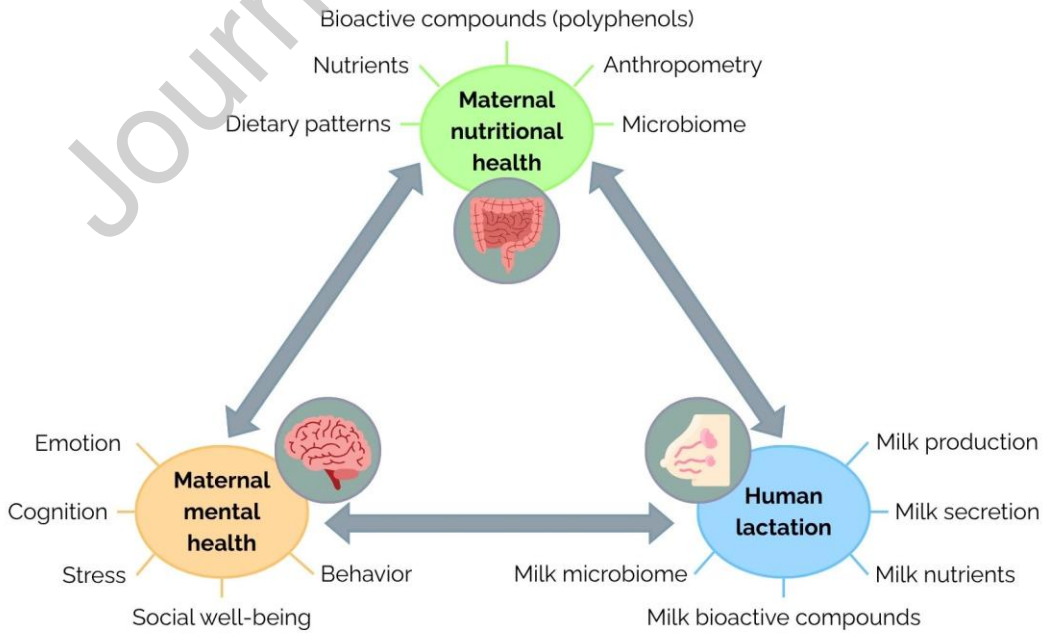
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CRediT Author Statement

A.R.M.: Conceptualization, Methodology, Investigation, Data Curation, Formal Analysis, Writing – Original Draft. P.E.B.: Methodology, Investigation, Data Curation, Formal Analysis, Writing – Review & Editing. S.V.S.: Supervision, Writing – Review & Editing. E.A.S.: Conceptualization, Methodology, Supervision, Project Administration, Funding Acquisition, Writing – Review & Editing.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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