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Discovering the Role of Human Milk Oligosaccharides in Neurocognitive Development

Breastmilk plays an important role in early life nutrition, providing a combination of nutrients and bioactive components essential for infant growth, development and long-term health. The primary components of breastmilk, including lactose, proteins and fats, serve as critical sources of energy and building blocks for the developing body. However, breastmilk is more than a source of calories, its bioactive components play important roles in supporting the immune system, gut health, and brain development.[1,2]

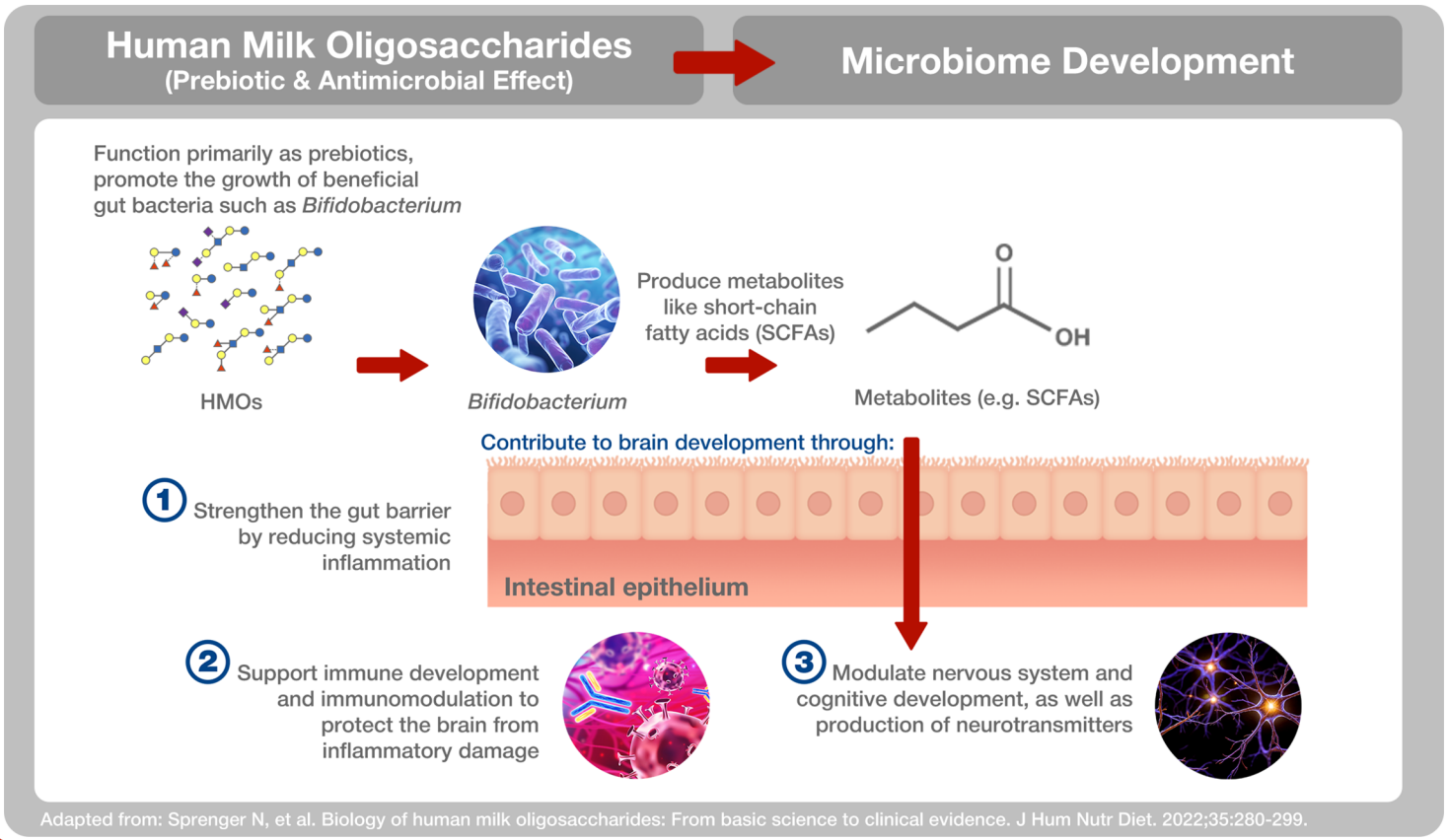
Brain development is a rapid, highly dynamic process in the early years of life, and serves as an important foundation for later cognitive abilities. Breastmilk supports cognitive development especially during this critical period of rapid brain maturation. Its bioactive components, including the human milk oligosaccharides (HMOs), play an integral role in the infant's learning potential and cognitive function.[3]

Human Milk Oligosaccharides are the third most abundant solid component in human milk. While these complex carbohydrates are largely indigestible by infants, they serve as substrates for specific species of bacteria in the infant gut. HMOs play a crucial role in supporting infant development by aiding gut maturation, shaping the gut microbiome, and strengthening the immune system.[1,2] Moreover, sialylated HMOs—those containing sialic acid—are particularly important for myelination, a key process in brain maturation that enables fast and efficient neural signaling.

HMOs Support Neurocognitive Development via Two Modes of Action

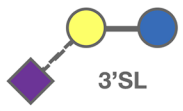
Emerging evidence highlights the role of HMOs in supporting neurocognitive development through 1) the interplay between the gut and immune systems and 2) the delivery of sialic acid via sialylated HMOs.[4]

1 Interactions Between the Gut and Immune Systems

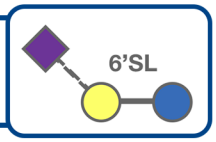


Adapted from: Sprenger N, et al. Biology of human milk oligosaccharides: From basic science to clinical evidence. J Hum Nutr Diet. 2022;35:280-299.

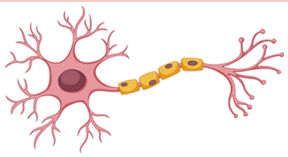
② Provision of Sialic Acid through Sialylated HMOs

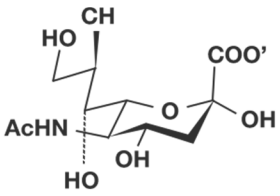


Sialylated HMOs, such as **3'-Sialyllactose (3'SL)** and **6'-Sialyllactose (6'SL)**, have specific roles in promoting brain development by providing **sialic acid**, a crucial building block for brain structures.[3]



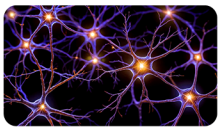
Supports myelin sheath formation for efficient signal transmission for rapid cognitive functions like learning and memory.[3]





Sialic Acid

Contributes to synaptic plasticity by aiding in the formation and remodeling of synapses for cognitive adaptability and problem-solving skills.[3]



Preclinical studies have highlighted the critical role of sialylated HMOs in cognitive development. One study demonstrated that the absence of dietary sialylated HMOs during early life leads to impaired cognitive functions, including deficits in attention, spatial and working memory. Another related study showed early-life supplementation with HMO blends positively influenced cognitive flexibility and memory development, particularly during the post-weaning period. These findings highlight the importance of dietary sialylated HMOs in shaping cognitive outcomes during early development.[5-6]

Observational Studies on Human Milk and specific HMOs in Infant Neurocognitive Development[3-7,12]

Several observational studies have highlighted how HMOs are associated with brain health benefits. It was also found that HMOs may have a role in the gut-brain connection and modulating cognition and brain development.

Early exposure (at 1 month and 6 months) to 2'-fucosyllactose (2'FL) was positively associated with cognitive development at 24 months.[3]

A positive correlation between 3'-sialyllactose (3'SL) and receptive and expressive language development in breastfed children aged 2 to 25 months.[7] 3'SL is associated with positive fine motor skills at 12 months.[8]

A significant correlation between 6'-sialyllactose (6'SL) and myelination at 3 months and social skills based on neuro-imaging and cognitive assessments at 12 months. Fucosylated HMOs linked to improved language outcomes.[8]

Specific HMOs (2'FL, 3'FL or 3'-fucosyllactose, 3'SL) promoted cortical gray matter and white matter maturation in infants.[9]

Positive association between 6´SL and cognitive and motor development at 18 months and a weaker association between 2´FL and motor outcomes at 6 months.[10]

Fucosylated and sialylated HMOs were positively associated with improved vocabulary at 18 months.[11]
Fucosylated HMOs associated with reduction in negative emotions in infants at 9 months.[8]

Higher 2'FL was associated with greater head growth and neurodevelopment at 1 month.[12]

In summary, breastmilk, with its unique components, is vital for infant growth, development, and long-term health. Among these, HMOs play an important role in shaping the gut microbiome, supporting the immune system, and promoting brain development. Specific HMOs, such as sialylated and fucosylated variants, have been linked to improved cognitive function and language development, highlighting their significance in fostering optimal neurocognitive development. A growing body of evidence suggests that HMO exposure in early life may be beneficial for neurodevelopment in infants.

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