

# Impact of feeding practices on the microbiome and posterior neuro-cognoscitive development and behaviour during the first 1000 days

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## ABSTRACT

The first 1000 days of the infant development are utmost important in the neuro-cognoscitive development of the individual; diverse factors modify the intestinal microbiome of the offspring, beginning with the characteristics of the mothers diet, mode of delivery, use of antibiotics, breastfeeding practice, moment of weaning, and many others; the purpose of this review is to state the diverse factors that affect the development of the microbiome and how it affects the brain functionality by altering the gut-brain interaction because of the changes regarding neurotransisor production and other changes regarding brain functionality and its posterior outcome on the cognoscitive development and behaviour.

**Keywords:** Childhood development, microbiome, enteric nervous system, central nervous system and breastfeeding.

## BACKGROUND

The first 1000 days of the infant development are utmost important in the neuro-cognoscitive development of the individual; it's a period where adequate nutrition must be guaranteed to prevent a deleterious impact on his/her development<sup>1</sup>. The absorption and digestion of nutrients that are received from the diet depends on the gut microbiome that is generated throughout the pass of time of the individual; modified during the beginning of the weaning and varies throughout the course of his/her development until it reaches to be the nearly the same as an adult<sup>2,3</sup>.

Complementary feeding is characterized by the diminished ingestion of milk and the introduction of solid food from different origins and depends on the certain characteristics of the parents, such as socioeconomically factors, education, doctor promotion or/and family knowledge of complementary feeding, ideas of infant hunger of the parents, this tends to promotes an early weaning<sup>4,5,6</sup>.

During the neonatal and early infant period nutrition starts to shape the microbiome; with later consequences on the individual's life<sup>7</sup>; the time of acquiring the different microbes influences on the development of the brain and its plasticity<sup>8</sup>.

Dietary antigens interact with the intestinal cells and the microbial community shaping it depending on the type of food ingested, if it is processed or farmed, if it is animal or vegetable based; these changes affect the production of metabolites that would flow to the blood stream and interact with the whole body<sup>2,7</sup>.

The bacteria that compose the gut microbiome are closely related with the enteric nervous system and the development of the glial cells in the gut lamina propia<sup>9,10</sup>; this system it's not fully developed on the first months of life, so it continues to grow and develop in relationship with the gut microbiome<sup>10,11</sup>, for that it depends on the characteristics of the food that infant receives and its structure varies throughout the time<sup>12</sup>; its function consists on the production of different neuro-transmisors that influence behavior of the individual<sup>9,13,14</sup>.

Depending the nutrients offered on the diet the gut microbiome modulates itself and affects the neurodevelopment of the individual, having effects on social, behavior and cognoscitive skills; thus when the gut microbiome changes so does the relation between the enteric nervous system and the central nervous system by altering the expression and effect of different neuro-active compounds that affect the brain development and/or interaction between neurons on the person; this changes persist in infancy through adulthood<sup>15,16,17,18</sup>.

Another way for interaction between the microbiome and the central nervous system is by involvement of the immune system<sup>19</sup>; with the generation of byproducts by the GI tract such as Short Fatty Acids (SCFA) producing multiple effects on the central nervous system by serving as energy compounds, neuro-transmisior or by generating epigenetic

changes by modulating the function of diverse enzymes such as histone deacetylases or affecting other neurotransmitter production; changes that will posteriorly modulate the development of the brain or the behavior of the individual and influence on the development of neurological diseases<sup>19,20,21</sup>.

### Neurotransmitters

The intestinal microbiome depending of the food ingested also produces GABA, serotonin, adrenalin, noradrenalin that influence the behavior of the individual, the production of those neuro-transmitters produce epigenetic changes on the brain that would influence on the behavior and the cognitive skills of the individual<sup>13,14, 21</sup>. It's been shown that serotonin agonist enhances cognitive skills facilitating learning and improves the individual's behavior<sup>22</sup>.

Serotonin protects the enteric nervous system from oxidative stress minimizing the risk of leaky gut syndrome, which would induce systemic stress affecting the proper functions of the CNS; also the production of serotonin from the gut induces later neural-protection and neural growth while affecting the activation of microglia<sup>23,24, 25</sup>.

Histamine it's a neuro-transmitter that influences the behavior of the infant and also on the properties of the intestinal mucosa; it is produced by the mast cells which also modify the properties of the intestinal mucosa and facilitate the migration of bacteria or by-products into the bloodstream, therefore affecting the development of the infant<sup>26,27</sup>.

### Childhood Development

The classic theory of Thomas and Chess states that the infant during its development has different traits that compose the temperament of him/herself; these intervene on the capacity to learn and obtain new skills in a faster or slower way as he grows<sup>28</sup>; these cognitive skills are in relation of the gut microbiome composition<sup>12</sup>.

During its childhood, the infant brain possess a high plasticity; this varies depending the actual neural networks and the ones that generate because the relation of the infant and its environment, changing the structure and its posterior abilities<sup>29</sup>. Just like the brain the gut microbiome depends on environmental factor in its development, such as the characteristic of foods, the moment of exposure in life and the duration of the exposure<sup>2,3,12,25</sup>, giving origin to an enteric nervous system that will relate with the central nervous system and gain the capacity to influence the behaviour of the individual and its cognitive abilities<sup>9,25</sup>.

The development of the enteric nervous system (ENS) occurs during the first months of life of the individual<sup>11</sup>, but the gut microbiome can continue to vary its composition until

it reaches the age of 3 years, when it's more similar to that of an adult<sup>12</sup>. The development of the ENS is closely related to the development of the central nervous system (CNS) so as the individual grows both structures change to obtain the best of their relationship. The microbiota adapts to offer the nutrients and substances for the development of both systems affecting the properties of them such as motility by the ENS, cognitive functions (learning, memory, emotions) and behavior of the individual by the CNS<sup>25,30,31</sup>.

Factor such as breastfeeding modulate the infant's microbiome and therefore its behavior by the continuous exposure of microbes, so when the withdrawal of them occurs before time the behavior of the individual changes; seen in mice that have been breastfed and weaned before time<sup>19</sup>, so the moment of weaning can influence on the behavior of the infant; the changes that occur throughout the weaning process are related more with the duration of the breastfeeding<sup>26</sup>. The diet of the mother during the pregnancy period such as the fat percentage affect the posterior outcome of the microbiome generating changes that will last even until the year of age affecting the posterior microbiome metabolism<sup>32</sup>.

Between the first and the second year of life it is recommended that the starts to learn to feed him/herself for the purpose of obtaining dietetic habits, this is closely related to feeding patterns before the year of life<sup>4,6</sup>.

In studies such as the one done by Grummer-Strawn et al<sup>33</sup> in 2008, it was found that 40 percent of the mothers initiated weaning before the 4 month of age and in the next 1 or 2 months introduce fruits as the next food; and that infants were fed on a high sugar high fat diet.

In another study by Morgan et al<sup>34</sup> in 2004 he found that the beginning of complementary feeding was associated with more weight gain, more height gain and increased cephalic perimeter, but the posterior was lost at the age 12 weeks.

Thompson et al found that depending the presence of breast feeding practice during the introduction of solid foods the microbiome will change or not more similar to that of an adult<sup>35</sup>.

Petra et al found that the characteristics of the microbiome and the activities of the mast cells influence on the person's behavior<sup>26</sup>.

Infants that had an early complementary feeding before the stipulated increased the number of side-effects such as acute watery diarrhea and the risk of chronic diseases in the adulthood<sup>5,31</sup>.

The repercussion of feeding and the nutritional state of the individual in the cognitive development turn more evident by the age of 9<sup>34</sup>.

## RECENT FINDINGS

It has been demonstrated then:

-That changes of the intestinal microbiome affect the behavior<sup>13,14,37</sup>.

-Food high in fiber influenced on the generation of neuro-active compounds that influence brain development<sup>15,25</sup>.

- Bacteria like Bifidobacterium and Lactobacillus influence positively on the individual's behavior<sup>17</sup>, and both of these bacteria are influenced by the consumption of breast milk.

-Depending on the nature of the food, be it animal or vegetable, processed or homemade, the number and type of microbes the food has changes and so the ability to colonize our gut changes<sup>38</sup>.

-Depending if the infant is exclusively breastfed or is fed with child formula during its first six months of life the intestinal microbiome changes, and an infant fed with breast milk its microbiome tends to produce more vitamin B than infants fed with infant formula because of the aforementioned changes<sup>39</sup>. Thus the changes in vitamin B concentration could modify the neurodevelopment of the infant.

-Epigenetic changes that occur on the brain by neurochemical reactions influence the neuro-progression of the brain and the posterior cognitive skills that start on infancy and persist throughout adulthood<sup>18,40</sup>, these changes are influenced by the migration of products generated by the intestinal microbiome that travels to the brain shaping gene expression<sup>20,21,41</sup>.

-The chemicals offered by the diet of an individual shape the intestinal microbiome and the synthesis of neurochemicals that modulate the behavior<sup>21,42</sup>.

-Fat percentage of the mother's diet modifies the outcome of the infant microbiome to bacteria with low affinity to metabolize complex polysaccharides<sup>32</sup>.

-The characteristics of the gut microbiome influence on the synthesis of myelin and brain microglia modifying the individual behaviors because of CNS modifications<sup>25,43</sup>.

-Psychoactive effects can take weeks to develop once the microbiome change has occurred and can continue for some weeks even though the bacteria that initiated the change disappears<sup>25</sup>.

-Breastfeeding and mode of delivery are factors that would influence the early colonization of the gut microbiota such as an initial variation of the intestinal microbiome profile and a posterior diversity of the intestinal microbiome<sup>44,45</sup>.

## CONCLUSION

The fetus and the mother co-exist as holobiont entities that will interact between affecting their microbiome niche; then with the arrival of the newborn the holobiont entity will

interact with its ecosystem in order for it to obtain the minimal obligatory gut metagenome that will be unique for each individual generating the traits that will differentiate between individuals<sup>46</sup>, such effects caused on the behavior and social interaction of the individual by microbiome changes can subsequently directly or indirectly alter the cognitive abilities, then generating changes on the diet and lifestyle that would continue to modify or stabilize the microbiome of the individual. Modifications of the microbiome in any point of an individual's life will alter the gut-brain axis and thus affecting the production of the different compounds synthesized by the gut that uses the brain such as amino-acids, vitamins and neurotransmitters. Studies proving these theories are based on animal models and not human models; so the need to research if feeding practices influence on the neuro-cognitive development and child's behavior can be proposed.

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