FETAL PROGRAMMING OF PSYCHOPATHOLOGY: THE ROLE OF GUT MICROBIOTA

GRECCHI A, BERALDO S
ASST-SANTI PAOLO E CARLO, PRESIDIO OSPEDALE SAN CARLO BORROMEO
SIP GIOVANI SEZIONE LOMBARDIA

Abstract

Epidemiological studies of birth and death records led to “Barker’s Hipopthesis” almost 30 years ago suggesting the influence of perturbed gestational milieu on the development of many chronic diseases later in life. Neurodevelopment is exquisitely sensitive to perturbation in the maternal milieu, including diet, infection and stress with long lasting behavioral consequences. Disorder such as schizophrenia, anxiety, depression and autism have been shown to be associated with in utero and early neonatal exposure to these stimuli. Infants exposed to antenatal stress demonstrate increased risk of developing a host of childhood and adult disease. While alteration of HPA axis and immune function have been the target of investigation as underlying mechanism conferring risk, the microbiome is an emerging candidate as a potential mediator of stress-induced pathogenesis.

We will discuss how the gut microbiota acts on the neurodevelopment through the action on the epigenetic trio (DNA, RNA and chromatin modifications) and its role in neurobehavioral programming of the immuno competence and how the microbiota shares some important characteristics in its interaction with the host that may compare to classical epigenetic mechanism (vertical transmission response to environmental stimuli, determination of gene expression programs and reversibility) in order to understand its implication in psychopathology.

Introduction

The emerging links between our gut microbiome and the central nervous system (CNS) are regarded as a paradigm shift in neuroscience with possible implications for not only understanding the pathophysiology of stress-related psychiatric disorders, but also their treatment.

Thus the gut microbiome and its influence on host barrier function is positioned to be a critical node within the brain-gut-axis.

Mounting preclinical evidence broadly suggests that the gut microbiota can modulate brain development, function and behavior by immune, endocrine and neural pathways of the brain-gut-microbiota axis.

Microbiota colonization

- According lifelong-standing dogs in biology, a mammal’s first contact with its microbiota occurs during birth in the birth canal. However, there is increasing body of evidence that demonstrates maternal transmission of certain microbes in utero, and thus the sterile-amos concept that is out-dated. Moreover, the mother’s gut microbiota changes dramatically during pregnancy.
- After delivery through the birth canal, the microbiota becomes more complex and abundant, and those community-level changes continue via breast-feeding and uptake of new microbes from the environment. It is not surprising that the microbiota critically influences pre-, peri- and postnatal development, and changes during early life stages will result in phenotypic alterations in adulthood.

The gut microbiota produces many neuroactive compounds, which can directly affect how neurons communicate with each other.

Among these are amino acids, (e.g., GABA and tryptophan), as well as monoamines, such as serotonin, histamine and dopamine, used as neurotransmitters in the brain or precursors of such.

However, there is accumulating evidence that also molecular epigenetic mechanisms are involved in shaping brain formation and functioning that can be influenced by microbial symbionts.

Bibliography


