Impact of the gut microbiota on brain development and function

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The gastro-intestinal tract hosts a complex microbial ecosystem, the gut microbiota (GM), whose collective genome coding capacity exceeds that of the host genome. The GM is nowadays regarded as a full organ, playing its part in the host physiology, and likely to contribute to the development of pathologies when its dynamic balance is disrupted (dysbiosis). In the last decade, evidence emerged that the GM influences brain development and function. Several studies comparing germfree (GF) and conventional laboratory rodents showed that the GM regulates the neuroendocrine and behavioural responses to stress. For example, we showed that GF rats subjected to an acute stress in an open-field test have an enhanced anxiety-like behaviour, a 3-fold higher serum corticosterone concentration, an elevated CRF mRNA expression in the hypothalamus and a reduced glucocorticoid receptor mRNA expression in the hippocampus, compared with conventional rats. Furthermore, the dysfunctions observed in GF animals can be corrected if the GM is restored in early life but not in adulthood, suggesting a critical period for microbiota imprinting on the responsiveness to stress. Besides, GF animals also show impairments of social behaviours, and alterations in neurotransmitters' turnover rates and in neurotrophic factors' gene expression in various brain regions. The modes of action are still to be deciphered. They may involve transport of neuroactive bacterial metabolites to the brain through the bloodstream, stimulation of the vagus nerve or of entero-endocrine cells, or modulation of the immune system and, consequently, of the inflammatory status. The discovery that the GM takes part to the gut-brain crosstalk paves the way for the hypothesis that GM dysbioses could contribute to the pathophysiology of brain diseases, including neurodevelopmental and psychiatric disorders. In this regard, manipulations of the GM through dietary interventions, mainly with probiotics, have proved to be effective in alleviating neurochemical, neuroendocrine or behavioural abnormalities in rodents. Nevertheless, future work is needed to determine whether brain function and behaviour changes related to microbiota in animal studies translate to humans.