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The gut-brain axis: interactions between *Helicobacter pylori* and enteric and central nervous systems

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Carabotti *et al* [1] suggested that gut microbiota has an important role in bidirectional interactions between the gut and the central nervous system (CNS). In this regard, we considered gastrointestinal immune system and brain dialogue, particularly implicated in neuroinflammation, as a common feature of the neurodegenerative and neuroinflammatory diseases [2].

Neuroinflammation might initiate from gastrointestinal track (GIT), a vulnerable area through which pathogens influence the brain. A proposed mechanism from GIT (i.e., "little brain") infections including *Helicobacter pylori* (*Hp*) current infection to the CNS (i.e., "big brain") neuroinflammation, is that the pathogen may access the brain through the blood, the oral-nasal olfactory and the faster GIT-associated retrograde axonal transport pathways [2,3]. Specifically, *Hp* induces relative mechanisms and/or mediators such as the synthesis of various cytokines and/or chemokines, which may be detrimental to the CNS inflammation and/or neurodegeneration. *Hp*, by inducing several inflammatory mediators such as tumor necrosis factor-α and interleukin (IL)-6, may contribute to blood-brain barrier (BBB) disruption leading to brain neurodegenerative diseases. In addition, *Hp*-induced vacuolating A cytotoxin exhibits chemotactic activities to the bone marrow-derived mast cells (BMD-MCs) and induces BMD-MCs to produce proinflammatory cytokines leading to BBB dysfunction; MCs can be stimulated by corticotropin releasing hormone, also mentioned by the authors [1], including histamine, IL-8, tryptase and vascular endothelial growth factor which disrupt the BBB. Likewise, human defensins might contribute to *Hp*-related brain pathologies by modulating innate and adaptive immune system responses. Finally, activated monocytes (possibly infected with *Hp* due to defective autophagy resulting in *Hp* replication in autophagic vesicles) might also access the brain due to BBB disruption (Trojan horse theory) contributing to *Hp*-related neurodegeneration [2-5].

Importantly, Hippocrates wisely remarked: "all the diseases begin in the gut" and "death sits in the bowel", thereby creating the hypothesis that gut is responsible for many disorders including neurodegenerative diseases.

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Conflict of Interest: None

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