이상운동질환에서 장-뇌 상호작용

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Gut brain interaction in Movement disorders

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Recent advances on the pathology of Parkinson's disease (PD) have turned light on the gastrointestinal tract as an early target of alpha-synucleinopathy. According to the Braak's hypothesis, vagus nucleus is the site of earliest involvement in PD pathology along with olfactory bulb, and the pathology of this disease is suggested to progress to the whole brain through caudal to rostral direction. Because of this, gut has been thought as a hot spot triggering Lewy body pathology of PD, and as supportively, incidental Lewy body disease cases with gut pathology has been reported. However, biopsy and surgical specimen studies in humans have shown some contradicting results depending on various staining methods and the anatomical sites of exams. With advances in the knowledge of the prion-like transmission of pathological alpha-synuclein throughout nervous system, experiments on PD primate models have shown that Lewy bodies containing alpha-synuclein species administered in the stomach could go upward to vagus nucleus and the nigrostriatal system as well whereas the striatal administration of Lewy bodies also resulted in enteric nervous system pathology in the stomach, thereby suggesting a bidirectional talk between gut and brain in the aspects of PD pathology. Epidemiologic researches shed light on the gastrointestinal disease, such as inflammatory bowel diseases and chronic H. pylori infection in association with increased risk of PD. Altered epithelial barriers induced by pro-inflammatory cytokines, dysbiosis, and alterations in the innate immune system via Toll-like receptors (TLRs) have been suggested as possible mechanisms for triggering alpha-synucleionopathy. Interestingly two well-known protective factors of PD, caffeine and smoking, are shown to have some anti-inflammatory effect in the gut, thereby suggesting as a modulatory effect on the gut level for the development of PD. H. pylori infection and its treatment-induced small intestinal bacterial overgrowth could lead to intestinal dysbiosis and bystander neuronal damage, provoking neurodegeneration in PD. Response to dopaminergic medications, plasma levodopa concentrations, and motor symptom severity of PD patients are reported to be associated with H.pylori infection, and there is a divergent effect on parkinsonian symptom relieved by H.pylori treatment. All these H. Pylori-related observations suggest an importance of gut-brain interaction in the treatment of PD in addition to the pathogenesis of Lewy body disease. Lastly, lots of microbiome researches on PD have been recently reported with showing another cosmos in this field while microbiome extract of PD subjects was shown to induce LB pathology in animal models. Application of probiotics, prebiotics, and synbiotics that could modulate TLRs is also undergoing investigation. In this session, current concept of Gut-Brain interaction in the pathogenesis and clinical progression of PD will be summarized.

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