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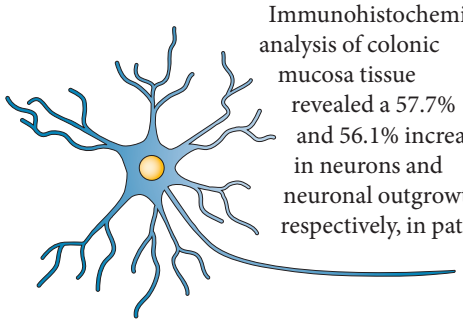
IBS

Mast cells cause nerves to sprout in patients with IBS

Infiltration of mast cells in the colonic mucosa of patients with IBS promote neuronal sprouting owing to the release of nerve growth factor (NGF), according to research published in *Gastroenterology*.

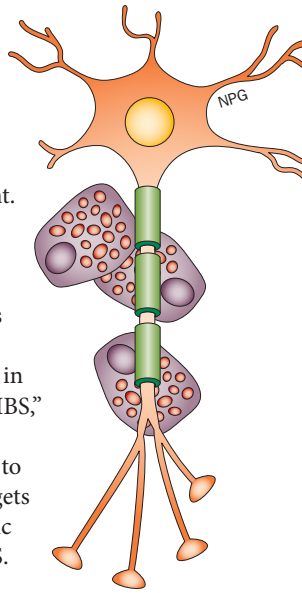
In previous studies, Giovanni Barbara and colleagues had demonstrated that the proximity of mast cells to enteric nerves correlated with abdominal pain in patients with IBS. In addition, they demonstrated that acute exposure of nerves to factors released from patients' colonic tissue altered neuronal activity. "We suspected that the chronic release of factors could affect the enteric nervous system and sensory fibres in a more structural way," explains Barbara.



Immunohistochemical analysis of colonic mucosa tissue revealed a 57.7% and 56.1% increase in neurons and neuronal outgrowth, respectively, in patients with IBS compared with healthy controls. Subsequent investigations revealed that NGF levels were 89.3% higher in patients with IBS than healthy controls.

"We hypothesized that mucosal mediators, particularly those released by mast cells, lead to neuronal sprouting," says Barbara. Double immunofluorescence staining of colonic tissue with NGF and the mast cell marker, tryptase, showed that the majority of cells expressing NGF also expressed tryptase. The high affinity nerve growth factor receptor, which binds NGF, was increased 193.8% in mucosal biopsy tissue from patients with IBS compared with controls.

In vitro experiments on primary cell cultures of the rat myenteric plexus and the neuroblastoma cell line SH-SY5Y, demonstrated an increase in neurite growth when exposed to supernatant made from mucosa affected by IBS. A similar level of neurite growth was seen in SH-SY5Y cells treated with 50 ng/ml of NGF. Furthermore, protein and mRNA expression of GAP43 (a marker of neuronal growth) was increased in rat myenteric neurons and SH-SY5Y cells when treated with IBS mucosal supernatant.



"These novel results ... pave the way to a new concept that structural abnormalities in the enteric nervous system could play a role in the pathophysiology of IBS," remarks Barbara.

The researchers hope to identify therapeutic targets to revert the neuroplastic changes observed in IBS.

Gillian Patman

Original article Dothel, G. *et al.* Nerve fiber outgrowth is increased in the intestinal mucosa of patients with irritable bowel syndrome. *Gastroenterology* doi:10.1053/j.gastro.2015.01.042