

MOTILITY

An enteric neuropathy might underlie diverticular disease

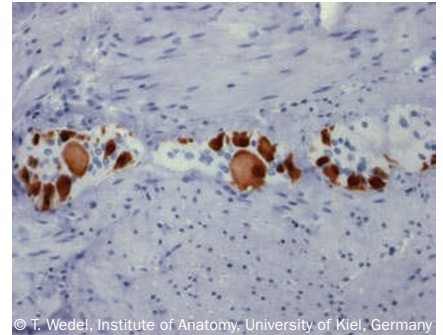
The pathogenesis of diverticular disease is multifactorial and poorly understood, although a low-fiber diet, connective tissue weaknesses and advanced age are known predisposing factors. However, a paradigm change may be in order: Thilo Wedel and colleagues propose that the mucosal herniations characteristic of diverticular disease might be the consequence of an underlying intestinal motility disorder related to distinct abnormalities of the enteric nervous system.

Wedel comments, “As the enteric nervous system is the key regulator of intestinal motility, our study evaluated the entire enteric nerve plexus to check whether enteric ganglia show histopathological abnormalities.” The researchers conducted a comprehensive morphometric analysis of colon samples from 27 patients with diverticular disease and 27 unaffected controls. Their approach utilized stringent new guidelines on histological reporting for gastrointestinal neuromuscular pathologies, which were published by an international working group in 2009.

Samples from patients with diverticular disease demonstrated an “overall neuronal shortfall ... in the myenteric and

submucosal plexus layers ... consistent with an oligoneuronal hypoganglionosis,” says Professor Wedel. Nearly half of the patients’ samples also showed an enteric gliosis of the myenteric ganglia. These features have not been consistently observed in previous morphometric studies of tissues affected by diverticular disease, in part because no standardized methodology or reliable normative data were available.

In their paper, the researchers suggest that a decline in enteric neurons to below a physiologically required threshold level could alter intestinal motor function as a result of compromised enteric neurotransmission. However, as yet, insufficient information is available to answer the question of whether this enteric neuropathy could potentially be the primary cause of diverticular disease or might develop secondary to other disease processes (such as muscular or connective tissue pathology, inflammatory injury or increased intraluminal pressure). Next, therefore, Wedel and colleagues plan to study the expression profiles of various neurotrophic factors responsible for the maintenance of the enteric nervous system. Depletion of these factors can result in complete or partial loss of enteric neurons.



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In the future, Wedel suggests, “researchers should keep in mind the increasing evidence that abnormalities of the enteric nervous system have a role in both the pathogenesis and generation of symptoms in diverticular disease.” These abnormalities, he continues, “could be considered as a target for novel therapeutic approaches,” in this debilitating disease.

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Original article Wedel, T. *et al.* Diverticular disease is associated with an enteric neuropathy as revealed by morphometric analysis. *Neurogastroenterol. Motil.* **22**, 407–414, e93–e94 (2009)