Neural plasticity is not only the adaptive response of the central nervous system to learning, structural damage or sensory deprivation, but also an increasingly recognized common feature of the gastrointestinal (GI) nervous system during pathological states. Indeed, nearly all chronic GI disorders exhibit a disease-stage-dependent, structural and functional neuroplasticity. At structural level, GI neuroplasticity usually comprises local tissue hyperinnervation (neural sprouting, neural, and ganglionic hypertrophy) next to hypoinnervated areas, a switch in the neurochemical (neurotransmitter/neuropeptide) code toward preferential expression of neuropeptides which are frequently present in nociceptive neurons (e.g., substance P/SP, calcitonin-gene-related peptide/CGRP) and of ion channels (TRPV1, TRPA1, PAR2), and concomitant activation of peripheral neural glia. The functional counterpart of these structural alterations is altered neuronal electric activity, leading to organ dysfunction (e.g., impaired motility and secretion), together with reduced sensory thresholds, resulting in hypersensitivity and pain. The present review underlines that neural plasticity in all GI organs, starting from esophagus, stomach, small and large intestine to liver, gallbladder, and pancreas, actually exhibits common phenotypes and mechanisms. Careful appraisal of
these GI neuroplastic alterations reveals that--no matter which etiology, i.e., inflammatory, infectious, neoplastic/malignant, or degenerative--neural plasticity in the GI tract primarily occurs in the presence of chronic tissue- and neuro-inflammation. It seems that studying the abundant trophic and activating signals which are generated during this neuro-immune-crosstalk represents the key to understand the remarkable neuroplasticity of the GI tract.