Provocation tests in functional gastrointestinal diseases – mechanistic diagnosis and therapeutic intervention

Gastrointestinal function is usually regulated by a complex network of reflex loops that renders digestive processing unnoticed, and only under abnormal conditions do sensory pathways become activated and symptoms develop. Symptoms arising in functional gastrointestinal disorders, including the irritable bowel syndrome, are currently considered to result from sensory-reflex disturbances in the gut (1). In turn, symptom perception conditions a behavioral response that may prompt the patient to visit a physician, among other things. This neurophysiologic concept admits that all functional disorders have a common pathophysiologic mechanism, and that specific clinical syndromes depend on the sensory and reflex pathways involved.

By definition, conventional diagnostic tests yield negative results in functional gastrointestinal conditions, and hence the reason why the sensory alarm became activated cannot be established. In order to try and unveil the source of symptoms provocation tests should be resorted to by applying a stimulus to the gut and then measuring specific responses. Reflex pathways may be activated using different types of stimuli; however, as physiologic stimuli escape perception, experimental stimuli such as gut distension should be resorted to in order activate sensory pathways under normal conditions. Three types of response may be assessed using these tests: perceived sensations, evoked responses at various levels in the nervous system, and reflex responses. Specifically, gut sensitivity may be assessed with various protocols (2), either by measuring the intensity of perception in response to a standardized stimulus or by establishing the stimulus threshold –i.e., the stimulus magnitude– for a given sensation such as distress or pain.

The goal to be reached with provocation testing is a mechanistic diagnosis identifying the sensory-reflex disturbance responsible for symptoms, which may include rectal hypersensitivity in patients with irritable bowel syndrome (3,4). However, as a secondary target, these tests may also modify the patient's behavior. Izquierdo et al. have shown how the identification of rectal hypersensitivity may influence the behavior of patients with irritable bowel syndrome in the long run, thus decreasing the demand for healthcare resources, particularly medical consultations (5). This finding is potentially highly significant because of its obvious socio-economic impact, and because it implies an improvement of patient status.

Well then, why does this effect occur? A major factor is probably the reproducibility of common symptoms by test stimuli. In fact, provocation tests have been shown to have the capability of inducing symptoms, which the patient recognizes as his or her usual complaints. Reproducibility probably results from an activation of specific pathophysiological mechanisms, and is particularly convincing because of its specificity. For instance, gastric –but not duodenal– distension reproduces usual

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discomfort in dyspeptic patients (6), and reproducibility in the various subgroups depends on the gastric area being stimulated (7). In patients with irritable bowel syndrome these changes only become apparent when distension stimulates mechanoreceptors, not when neural electrical stimulation is used in that same area of the intestine (8). Therefore, there is seemingly some specificity according to the location and type of stimulated pathways.

By reproducing clinical symptoms, patients themselves realize the mechanism underlying their discomfort, and this learning will condition subsequent responses. That is, provocation testing has a feedback effect that is typical of biofeedback therapies. Biofeedback is an operant conditioning technique by which the patient is made aware of biological responses so that he or she may then modify them. As such, biofeedback may be used in various settings such as, for instance, the correction of defecation maneuvers in patients with constipation due to expulsion difficulty. In patients with irritable bowel syndrome, an understanding of mechanisms underlying symptoms undoubtedly contributes to decreasing uncertainty on the origin of discomfort. It must be borne in mind that cognitive factors directly influence sensory-motor function and symptom production. Factors such as attention, hypervigilance or stress have been shown to enhance the perception of digestive stimuli (9), and this may be particularly relevant in hypersensitive patients. Furthermore, cognitive factors may also modify the way in which the patient responds to symptoms, thus influencing his or her behavior, and particularly his or her demand for medical care.

Interacting with patients is a major asset in the treatment of irritable bowel syndrome, as they may be educated on the nature of their symptoms and helped to modify their coping strategies; in this sense, provocation testing may well act as a therapy modality. Given the frequency and huge expenses entailed by this sort of disturbance, the economical impact of the finding by Izquierdo et al. may be significant. Moreover, if functional gastrointestinal conditions share a common pathophysiology, these conclusions may be extended to other syndromes, such as functional dyspepsia, with similar epidemiologic and socio-sanitary characteristics.

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