



Solving the Biopsychosocial Puzzle in Functional Dyspepsia

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By: Lukas Van Oudenhove, M.D., Ph.D., Professor, Translational Research Center for Gastrointestinal Disorders, KU Leuven Department of Clinical and Experimental Medicine, University of Leuven, Belgium



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Functional dyspepsia is the most prevalent functional gastrointestinal disorder (FGID) of the upper gastrointestinal (GI) tract. The disorder can significantly impact the quality of life of those affected.

Dyspeptic symptoms may develop due to diseases such as peptic ulcer or gastritis. However, most people with dyspeptic symptoms that are ultimately diagnosed have functional dyspepsia.

A diagnosis of functional dyspepsia is made on the basis of the presence of a group of symptoms that frequently occur together, in the absence of any structural or metabolic disease likely to explain the symptoms. The symptoms are thought to originate in the upper digestive tract (stomach and upper small intestine), and are felt in the middle upper part of the abdomen, below the breastbone and above the navel (epigastric region).

The symptoms most often include feelings of:

- Burning
- Pain
- Fullness after the meal
- Early satiation

Functional dyspepsia can be further subdivided based on, 1) symptoms which are most often *not* meal-related, such as epigastric pain and burning (epigastric pain syndrome), and 2) symptoms which *are* meal-related, particularly early satiation and fullness after the meal (postprandial distress syndrome).

The exact causes of functional dyspepsia are not known and likely a variety of causes can lead to symptoms. The symptom patterns can vary among individuals and multiple factors may interact in each person to shape their symptom expression. These all make treating the disorder challenging.

The biopsychosocial model looks at functional dyspepsia, like other FGIDs, as the result of complex interactions between biological, psychological, and social factors. Our research group, at the University of Leuven in Belgium, has been trying to unravel the role of these different factors in functional dyspepsia.

Gastric Sensorimotor Function

Gastric (stomach) sensitivity, accommodation, and emptying are collectively called gastric sensorimotor functions.

Gastric Sensitivity – About 4 in 10 people with functional dyspepsia experience epigastric pain or other symptoms at lower volumes of distension of the stomach than healthy people who do not have dyspepsia.

Gastric Accommodation – Gastric accommodation is the relaxation of the stomach upon meal intake. This relaxation allows an increase in volume without an increase in pressure. In about half of individuals with functional dyspepsia the stomach does not relax properly. This is linked to symptoms of early satiation.

Gastric Emptying – Delayed gastric emptying is found in roughly 1 in 3 individuals with functional dyspepsia. This is associated with fullness after the meal. Delayed gastric emptying is also associated with the symptoms of nausea and vomiting, which are *not* typical symptoms of functional dyspepsia.

The role of delayed gastric emptying in functional dyspepsia symptom expression is unclear. Increasing gastric emptying with the use of prokinetic/promotility drugs does not consistently improve dyspeptic symptoms.

Our research suggests that these different functions may not act independently. They may influence each other in a complex, and yet unknown, fashion.

Psychosocial Factors and Psychological Disorders

A link between normal and abnormal psychological factors (for example, daily stress and anxiety or depression) and abdominal symptoms has long been recognized. Modern research on the role of psychosocial factors in functional dyspepsia started with the adoption of generally accepted diagnostic criteria in the late 1980s to early 1990s.

The majority of studies suggest a higher than average prevalence of anxiety and depression in individuals with functional dyspepsia. While this suggests that anxiety and depression play a role in functional dyspepsia it is not known whether they contribute to functional dyspepsia symptoms, or vice versa.

I strongly believe it is not productive to think about the relationship between psychological factors and functional dyspepsia symptoms in terms of simple cause and effect. Instead, interactions in both directions are likely to be at play. Where warranted, a multidisciplinary approach to the treatment of functional dyspepsia symptoms that targets psychological factors and GI function simultaneously is appropriate. Our research group at the University of Leuven has tried to better understand this relationship.

Interactions between Psychological Factors, Gastric Function, and Symptoms

To study these complex interactions, we obtained data on biological (gastric sensorimotor function), psychological, and social factors, and functional dyspepsia symptom levels from a large group of individuals seen at our specialized (tertiary) medical referral center.

We found that both sensory and motor function in the stomach can be influenced by psychosocial factors or by psychological processes. We observed an association between anxiety levels with gastric hypersensitivity, and prior trauma associated with both gastric sensitivity and emptying.

Our recent work demonstrates that anxiety levels are associated with impaired accommodation in a large group of people with functional dyspepsia. Psychological functioning and gastric sensorimotor function appear to interact in a complex way. The presence of one does not exclude a role of the other. We demonstrated that physical symptom reporting is the result of a complex interaction between several groups of psychosocial factors and gastric sensitivity.

Additionally, we studied how gastric sensation is processed in the brain in people with functional dyspepsia compared to healthy people without dyspepsia.

It is important to distinguish between brain regions and networks where bodily signals are *processed* and brain circuitry where activity in the processing regions is *modulated* (altered), including emotional and cognitive circuits. Perception of gastric signals is the result of the interaction between these two brain networks. Abnormalities in these mechanisms may underlie symptoms in functional dyspepsia in general, and the influence of psychosocial factors on symptoms in particular.

In our study, hypersensitivity of gastric sensations in individuals with functional dyspepsia showed activity patterns in similar pain processing regions as healthy controls, but at far lower gastric pressure thresholds.

Furthermore, we found lack of activation of an important pain modulatory region of the brain (anterior cingulate cortex) during gastric distension in individuals with functional dyspepsia. This may underlie the increased signaling in the

pain processing regions. Anxiety was also found to interfere with the function of the pain modulatory region.

Finally, we demonstrated that a history of severe trauma (represented by physical or sexual abuse) in individuals with functional dyspepsia affects the function of a number of important pain processing and modulatory regions of the brain.

Summary

Functional dyspepsia describes a set of symptoms in the upper abdomen shaped by a complex interaction between biological, psychological, and social factors. We are gradually gaining insight into the nature of these interactions as well as the neuro-biological mechanisms underlying them. This warrants a biopsychosocial approach to the definition, diagnosis, and treatment of functional dyspepsia.

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537 Long Point Road, Suite 101
Mt Pleasant, SC 29464

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