Acute Anxiety and Anxiety Disorders Are Associated With Impaired Gastric Accommodation in Patients With Functional Dyspepsia

Huynh Giao Ly,[*,a] Nathalie Weltens,[*,a] Jan Tack,[*,b] and Lukas Van Oudenhove[*,‡,b]

*Translational Research Center for Gastrointestinal Disorders, Department of Clinical and Experimental Medicine, University of Leuven, Leuven, Belgium; ‡Psychiatry, University Psychiatric Centre KU Leuven, University Hospitals Leuven, Leuven, Belgium

BACKGROUND & AIMS: **Functional dyspepsia (FD) is associated with impaired gastric accommodation, as well as gastric hypersensitivity, delayed emptying, and psychosocial comorbidities. In healthy people, acute anxiety impairs gastric accommodation, measured as the average increase in gastric volume after a meal over 1 hour. This measurement approach does not address the complex time course of the gastric accommodation response to a meal. We modeled gastric accommodation in patients with FD as a function of postprandial time, to investigate whether it is associated with psychosocial factors (state anxiety, anxiety disorder, depression) and gastric sensorimotor function (sensitivity, emptying).**

METHODS: **We studied gastric sensorimotor function in 259 consecutive patients diagnosed with FD based on Rome II at the University Hospitals Leuven from January 2002 through February 2009. Subjects underwent a gastric barostat and breath test; psychosocial status was assessed by questionnaires. Subjects completed the State-Trait Anxiety Inventory to measure levels of state anxiety immediately before and after gastric barostat analysis. The time course of the accommodation response was analyzed using mixed models. Psychological and sensorimotor variables were added to the model as continuous (state anxiety) or dichotomous (gastric sensitivity and emptying, anxiety disorders, depression) covariates, including their interaction with the time effects.**

RESULTS: **In subjects with FD, delayed emptying ($\beta = 50.3 \pm 15.9$; $P = .002$) and lower state anxiety ($\beta = -1.7 \pm 0.7$; $P = .012$) were associated with an upward shift of the accommodation curve. There was a significant interaction between comorbid anxiety disorder and linear ($\beta = 8.2 \pm 3.5$; $P = .02$), quadratic ($\beta = -0.4 \pm 0.1$; $P = .004$), and cubic ($\beta = 0.005 \pm 0.002$; $P = .002$) effects of time: patients with a comorbid anxiety disorder had significantly slower initial increases in gastric volume to a lower maximum, and a slower return to baseline, compared with patients without anxiety disorder. Depression and gastric sensitivity were not associated significantly with gastric accommodation.**

CONCLUSIONS: **In patients with FD, state anxiety and comorbid anxiety disorders are associated with impaired accommodation; gastric emptying also is associated with accommodation in these patients. These findings help elucidate the complex interactions between psychological processes and disorders, gastric sensorimotor dysfunction, and symptom reporting in patients with FD.**

Keywords: Psychology; Postprandial Distress; Epigastric Pain; Functional Gastrointestinal Disorders.

Functional dyspepsia (FD) is defined by Rome III criteria as the presence of symptoms thought to originate in the gastroduodenal region in the absence of structural or metabolic disease that explains these symptoms.[1] FD is a syndrome with a multifactorial etiology and pathogenesis that likely results from interactions between biological, psychological, and social factors.[2–4] First, FD is associated with gastric sensorimotor dysfunction (impaired gastric accommodation to a meal, hypersensitivity to gastric distension, and delayed

[a]Authors share co-first authorship. [b]Authors share co-senior authorship.

Abbreviations used in this paper: ANS, autonomic nervous system; DSS, dyspepsia symptom severity; EPS, epigastric pain syndrome; FD, functional dyspepsia; GI, gastrointestinal; HC, healthy control; PDS, postprandial distress syndrome.

1542-3565/$36.00
http://dx.doi.org/10.1016/j.cgh.2015.03.032

gastric emptying).[4] Second, FD is associated with psychological status alterations (including depressive and anxiety disorders comorbidity).[3]

Gastric accommodation is a vago-vagal reflex initiated by the arrival of nutrients in the stomach and duodenum and resulting in fundus relaxation (decreased proximal stomach tone), which creates storage capacity for food without pressure increase, thereby enabling the gastric fundus to exert its reservoir function.[5]

Gastric accommodation commonly is measured using a gastric barostat, and quantified as the difference in intraballoon volume 30 minutes before and 60 minutes after a standardized liquid meal at fixed intraballoon pressure.[5] Based on this quantification method, approximately 40% of FD patients have impaired accommodation,[5] which has been associated consistently with the postprandial distress symptoms (postprandial fullness, early satiation) of the FD syndrome.[2,5] However, this approach ignores the complex time course of the gastric accommodation response, which may result in low statistical power to detect differences between groups or relationships with other relevant etiopathogenetic factors within the heterogeneous FD group. Even without taking these methodologic issues into consideration, research on how other gastric sensorimotor processes and psychosocial comorbidity may be associated with gastric accommodation in FD is virtually nonexistent. However, we previously showed that experimentally induced anxiety significantly impairs gastric accommodation in healthy volunteers, providing proof of concept for central influences on this vago-vagal reflex.[6]

Therefore, our primary aim was to model the time course of the gastric accommodation response and use this approach to investigate the putative association between gastric accommodation and other key gastric sensorimotor functions (sensitivity, emptying) as well as psychosocial status (state anxiety, comorbid depressive and anxiety disorders). Based on our study in healthy volunteers,[6] we hypothesized an association between increasing state anxiety as well as the presence of comorbid anxiety disorders and impaired accommodation (downward shift or lower maximum of the initial postprandial volume increase). Given the lack of prior evidence, no specific a priori hypotheses were formulated for gastric sensitivity, emptying, and presence of comorbid depressive disorder. Our secondary aim was to apply this analysis method to confirm differences in gastric accommodation between healthy controls and FD patients, and an association between postprandial distress symptom levels and impaired accommodation.

Methods

Participants

Consecutive Dutch-speaking Rome II FD patients with a recent diagnosis (either at their visit to the general gastrointestinal [GI] or GI motility clinic at the University Hospitals Leuven, or at a recent secondary care gastroenterologist visit that lead to referral to our center) were recruited between January 2002 and February 2009. The patient sample of the present study partially overlapped with recent studies from our group.[7–9] However, the hypotheses tested in the present study were novel and the results have not been reported elsewhere.

Healthy volunteers who participated in gastric barostat studies in which no drugs were administered were used as controls.

Details on patients and healthy controls are provided in the Supplementary Methods section. Q14

Gastric Barostat Protocol

Gastric sensitivity to distension and gastric accommodation were studied using a gastric barostat. Details are provided in the Supplementary Methods section.

Gastric Emptying Measurement

Gastric half-emptying time for solids was calculated using the ^{14}C octanoic acid breath test. The validated cut-off time of 109 minutes was used to define delayed emptying.[10]

Psychometric Questionnaires

On the day of the barostat investigation, FD patients filled out the following self-report questionnaires.

Dyspepsia Symptom Severity Scale. The severity of dyspeptic symptoms was evaluated using the Dyspepsia Symptom Severity (DSS) scale, consisting of Likert scales (range, 0–3: absent, mild, moderate, or severe) on the intensity of 9 dyspeptic symptoms during the past 3 months. The DSS is calculated as the sum of all 9 items.[11]

Because patient recruitment started years before the introduction of the Rome III criteria in 2006, no data on the subdivision of FD in the Epigastric Pain Syndrome (EPS) and/or Postprandial Distress Syndrome (PDS) are available. However, to test the association between the time course of the accommodation response and EPS and PDS symptom levels, EPS symptom severity was quantified by calculating the sum of the epigastric pain and epigastric burning items of the DSS; PDS symptom severity was calculated as the sum of the postprandial fullness and early satiation items. For analysis purposes, the resulting ordinal variables (0–6) were dichotomized by median split.

State-Trait Anxiety Inventory, state scale. The state scale of the State-Trait Anxiety Inventory[12,13] was filled out twice, immediately before and after the barostat investigation (with the latter rating referring retrospectively to the period during the barostat investigation).