

Functional Nausea, Gut, Brain, or Both?



The gut-brain pathways for nausea, distinct from those for vomiting, involve the convergence of the central and autonomic nervous system, endocrine, and gastrointestinal systems.^{1,2} Although vomiting is mediated through the brainstem and considered a motor response, nausea has sensory, cognitive, psychological, and homeostatic influences that trigger a response from the limbic system.³ The functional brain network for nausea is wide and the morphology of the subcortex (amygdala, caudate, and putamen) has been associated with the severity of nausea.² Various signals like visual, vestibular, auditory, gustatory, olfactory, orthostatic, visceral, somatosensory, and proprioceptive can stimulate nausea.

Nausea, an accompanying symptom in about two-thirds of childhood functional abdominal pain disorders, is associated with impaired functioning and worse gastrointestinal and psychosomatic symptoms that can progress to adulthood.⁴⁻⁸ Chronic nausea has often been an overlooked symptom. The Rome 4 criteria recognized functional nausea as a separate entity. These include at least 2 months of (1) predominant symptom of bothersome nausea at least twice per week, and most of the time is not related to meals, (2) not consistently associated with vomiting, and (3) after appropriate evaluation, nausea cannot be fully explained by another medical condition.⁹

In this volume of *The Journal*, Tarbell et al report their comprehensive review of the comorbidities and the diagnostic workup involved in patients with functional nausea.¹⁰ They have combined prospective and retrospective approaches utilizing specific questionnaires and review of the electronic medical records. There has been an evolving interest in functional gastrointestinal disorders, joint hypermobility, and orthostatic intolerance.¹¹⁻¹³ The authors have previously published the relationship between orthostatic intolerance and chronic nausea.^{14,15} In the present report, they find high rates of abdominal pain and vomiting, and a plethora of extraintestinal symptoms, including headache, orthostatic intolerance, hypermobility, fatigue, disturbed sleep, allergies, and anxiety. The somatic associations described are similar to those described in the previous literature on nausea in functional abdominal pain disorders.⁴ The authors have mapped out the breadth of these overlapping conditions, emphasizing the need for a multidisciplinary treatment approach.

The authors have attempted a thorough exploration of the diagnostic workup involved in functional nausea. They find a low yield for endoscopic, radiologic, and surgical interventions to establish a clear etiology for nausea. This finding may be in part because the pathophysiology of nausea is not fully elucidated and the current tests have limitations in providing management guidance. For example, patients

with nausea can have either normal or delayed gastric emptying; thus, scintigraphy has limited clinical usefulness. They report some benefit for the head-up tilt testing to diagnose postural orthostatic tachycardia syndrome or orthostatic hypotension in patients with high clinical suspicion and recommend it as an adjunct if needed. The clinical significance of autonomic testing remains unclear, because it has not been validated for nausea and there is a lack of data on healthy subjects. In addition, there are discrepancies in institutional testing protocols and there is a need for standardization through rigorous scientific studies.

Inadequate value-based care has become an ongoing concern and millions of healthcare dollars are spent on avoidable studies and procedures, especially for functional gastrointestinal disorders.^{4,16} There is a tendency to focus on elaborate gastrointestinal evaluations with little attention to the comorbidities accompanying nausea. The authors deliver an important message encouraging the diagnostic clinician to expand their outlook toward nausea beyond the gastroenterology toolbox and reduce the healthcare cost burden as well as risk to patients from extensive investigations.

Nausea may have deeper ramifications than those currently known that encompass multifaceted mechanisms. The authors have made a great start to unravel the complexities of functional nausea. The overlay of dysautonomia, postconcussive symptoms, vagal nerve insufficiency, and circadian rhythm disturbances remains obscure. The role of the microbiome, neuroimmune, and hormonal regulation is yet to be explored. It would be prudent to direct future studies to identify the different phenotypes of nausea so that treatments like pharmacotherapy, psychological interventions, and neuromodulation can be tailored to individual populations. ■

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With a Grain of Salt: Can We Make a Difference?



Salt is a plentiful and inexpensive preservative, and its use is noted in historical texts dating back many centuries.¹ Although our bodies require a modest amount of salt (in the form of NaCl) to function normally, it seems too easy in modern times to get much more than is needed, with resulting health problems such as hypertension and other cardiovascular complications. Within the definition of “salt” in the Merriam-Webster online dictionary, one finds that skepticism might be described as “with a grain of salt,” leading one to wonder about the advice given to patients at times.²

A recent experience in a hypertension clinic pointed out the challenges confronted by patients who try to follow the advice they have been given. A teenage boy who has been followed for a couple years mentioned that he was having headaches. He is an average-sized teenager, an athlete and a good student with a family history of hypertension. He monitors his blood pressure at home and brings in a log of recordings at visits. He takes a small dose of one medication, which controls his blood pressure. As we discussed his headaches, he finally volunteered: “Doc, they tend to happen at the end of the day, and I think it’s because I get hungry.” Asking further about his breakfast and lunch habits, he also volun-

teered that he skips those meals, because “the food they serve isn’t on the diet I’m supposed to follow.” Who might be more skeptical, patient or doctor?

In this volume of *The Journal*, Rich et al report their analysis of data from more than 16 000 children and adolescents collected in the US National Health and Nutrition Examination Surveys (NHANES) from 2003 to 2016. The authors analyzed the sodium intake of these individuals.³

Despite widespread efforts at the national level to reduce the intake of sodium, whether the recommendations from the US Department of Agriculture (USDA) have had any impact is not clear. Rich et al provide insight into the sodium consumption of the pediatric population. The USDA has recommended reduced sodium consumption for a quarter of a century, and age-specific guidelines have been in effect for a decade. Yet, the findings of this analysis tell a different story. The authors reviewed the intake of a large cohort of children and adolescents aged 4-17 years, split almost evenly between males and females, using NHANES surveys for 2003-2016. Along with looking at the entire group, they also examined subsets of the group by age, sex, race, and ethnicity.

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NHANES National Health and Nutrition Examination Survey
USDA US Department of Agriculture

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