



Review

What is nausea? A historical analysis of changing views

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ARTICLE INFO

Article history:

Received 4 May 2016

Received in revised form 11 July 2016

Accepted 13 July 2016

Keywords:

Nausea

Vomiting

Emesis

Sopite syndrome

Seasickness

ABSTRACT

The connotation of “nausea” has changed across several millennia. The medical term ‘nausea’ is derived from the classical Greek terms *ναυτία* and *ναύουα*, which designated the signs and symptoms of seasickness. In classical texts, nausea referred to a wide range of perceptions and actions, including lethargy and disengagement, headache (migraine), and anorexia, with an awareness that vomiting was imminent only when the condition was severe. However, some recent articles have limited the definition to the sensations that immediately precede emesis. Defining nausea is complicated by the fact that it has many triggers, and can build-up slowly or rapidly, such that the prodromal signs and symptoms can vary. In particular, disengagement responses referred to as the “sopite syndrome” are typically present only when emetic stimuli are moderately provocative, and do not quickly culminate in vomiting or withdrawing from the triggering event. This review considers how the definition of “nausea” has evolved over time, and summarizes the physiological changes that occur prior to vomiting that may be indicative of nausea. Also described are differences in the perception of nausea, as well as the accompanying physiological responses, that occur with varying stimuli. This information is synthesized to provide an operational definition of nausea.

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Contents

1. Introduction	5
2. Historical perspectives on nausea: cross-cultural insights into a definition	6
3. Prodromal physiological changes: Potential physiological markers for nausea	10
3.1. Mechanisms of nausea and vomiting	10
3.2. Prodromal responses: general considerations	11
3.3. Prodromal responses: gastrointestinal system	11
3.4. Prodromal responses: endocrine system	12
3.5. Prodromal responses: central nervous system and autonomic nervous system	12
3.6. Prodromal responses: non-emetic animals	13
4. An operational definition for nausea	13
Acknowledgements	14
References	14

1. Introduction

Although the expulsion of gastric contents through vomiting is easy to recognize, the sequelae of physiological responses that precede this response are less clear-cut. Money divided the physiological events

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associated with vomiting into two categories: stomach-emptying responses and stress responses (Money, 1970; Money et al., 1996). The latter term has mainly been used to describe responses such as cold-sweating (Cheung et al., 2011; Hemingway, 1944; Nobel et al., 2012; Sclocco et al., 2015) and pallor (Cassano et al., 1989; Kolev et al., 1997) that often occur following exposure to emetic stimuli, which are mediated through the sympathetic nervous system (Hammam et al., 2012). However, other physiological changes may be associated with the pre-emetic stress response, including alterations in heart rate variability (Doweck et al., 1997; Kim et al., 2011, 2005) and a release of vasopressin from the posterior pituitary (Fisher et al., 1982; Robertson, 1976; Rowe et al., 1979; Sorensen and Hammer, 1985). Along with these physiological responses are a number of perceptions with accompanying behavioral changes (Graybiel et al., 1968; Muth et al., 1996), including an awareness that stomach emptying is imminent, loss of appetite (Farmer et al., 2015; Heer and Paloski, 2006; Hiura et al., 2012; Lackner, 2014; Sanger et al., 2013), anxiety and foreboding (Coelho and Balaban, 2015; Fox and Arnon, 1988; Lackner, 2014; Tarbell et al., 2014), as well as lethargy and disinterest in engaging in routine activities (Graybiel and Knepton, 1976; Lackner, 2014; Lawson and Mead, 1998; Matsangas and McCauley, 2014; Van Ombergen et al., 2015). The latter disengagement responses were first documented by Graybiel and Knepton (1976), and later described by others, who referred to them as the “sopite syndrome” (Graybiel and Knepton, 1976; Lackner, 2014; Lawson and Mead, 1998; Matsangas and McCauley, 2014; Van Ombergen et al., 2015).

Nausea is the term that is used to describe an awareness that vomiting is imminent. However, individuals often experience nausea without vomiting (Horn, 2014; Lackner, 2014). Moreover, individuals describe nausea in various ways (Graybiel et al., 1968; Muth et al., 1996), in accordance with the wide range of perceptions that can occur prior to vomiting. For example, over 30 definitions of nausea were provided in a recent book on the topic (Stern et al., 2011).

Nausea and emesis have a number of etiologies, including motion-related signals that deviate from those expected, administration of toxins, exposure to radiation, migraine, gastrointestinal disease, pregnancy (hormonal changes), and even psychological stimuli (e.g., stress and extreme emotional reactions, as well as classically conditioned smell and taste aversions) (Feyer et al., 2014; Hederes, 1992; Heer and Paloski, 2006; Horn et al., 2014; Kenward et al., 2015; Matthews et al., 2014; Olden and Crowell, 2005; Singh et al., 2016; Sugino and Janicki, 2015; Wiesmann et al., 2015; Yates et al., 2014). There is some evidence that the prodromal signs and symptoms preceding vomiting can vary depending on the emetic trigger. For example, the sopite syndrome has mainly been associated with motion sickness (Graybiel and Knepton, 1976; Lackner, 2014; Lawson and Mead, 1998; Matsangas and McCauley, 2014; Van Ombergen et al., 2015). In some cases, prodromal signs and symptoms build-up slowly and have a long duration; in others, vomiting occurs suddenly after an emetic stimulus, such that prodromal signs and symptoms are of short duration (Katelaris and Jones, 1989; Kovacic and Chelimsky, 2014; Lackner, 2014; Metz and Hebbard, 2007; Olden and Crowell, 2005). These complexities have confounded the description of nausea in the literature.

Since nausea is a perception, a verbal report of a patient is required to ascertain if they are nauseated. However, it is often desirable to establish whether nausea is present, or if vomiting is likely, in individuals who cannot report their sensations (e.g., pediatric and postoperative patients) as well as animal subjects used in experiments to develop anti-nausea agents. This review provides historical perspectives on the definition of “nausea,” as well as a summary of the physiological changes that occur prior to vomiting that may be indicative of nausea. Also described are differences in the description of nausea, as well as the accompanying physiological responses, that occur with varying stimuli. This information is synthesized to provide an operational definition of nausea.

2. Historical perspectives on nausea: cross-cultural insights into a definition¹

The definition of the sensation (or symptom) of nausea has its roots in ancient medicine. Historical perspectives on “nausea” are broader than contemporary definitions, which often classify nausea as a precursor or predisposing factor for vomiting. For example, Dorland's Illustrated Medical Dictionary (Anon., 1988) defines nausea as: “an unpleasant sensation, vaguely referred to the epigastrium and abdomen, and often culminating in vomiting.” Similarly, an earlier dictionary defined nausea simply as “tendency to vomit; sickness at the stomach” (Dorland, 1929). There are more expansive original meanings of “nausea,” though, that provide a conceptually richer context for understanding this sensation, its perceptual dimensions, its time course, and potential underlying biological mechanisms.

After experiencing a bout of seasickness, the American classics scholar John Carew Rolfe published a comprehensive guide to Greek and Latin references about seasickness (Rolfe, 1904). His publication provides a useful and comprehensive summary of the usage of the word ‘nausea’ and related terms in classical texts. The medical term ‘nausea’ is derived from the classical Greek terms *ναυτία* and *ναύουα*, which designated the signs and symptoms of seasickness. The term was adopted in Latin as the loan words *nausea*, *nausia* and *nautea*, which designate manifestations of seasickness or, more figuratively, mean “a qualm” (Lewis and Short, 1879) or “a sense of queasiness.” In fact, the definition encompassed the symptom clusters for early motion sickness that have been termed the ‘sopite syndrome’ (Graybiel and Knepton, 1976; Lackner, 2014; Lawson and Mead, 1998; Matsangas and McCauley, 2014): excessive drowsiness, lassitude, lethargy, degraded ability to concentrate on tasks, disinclination for mental or physical work and signs of mild depression.

The contextual richness of this definition can be appreciated from a passage from a letter (Epistle 53, 1st century CE) written by the Roman philosopher Lucius Seneca (Seneca, 1917) about a bout of seasickness:

“Peius autem vexabar, quam ut mihi periculum succurreret. Nausia enim me segnis haec et sine exitu torquebat, quae bilem movet nec effundit.”

I was suffering too grievously to think of the danger, since a sluggish seasickness [Nausia] which brought no relief was racking me, the sort that upsets the liver without clearing it. (p 353–354)

The meaning of the reference to ‘upsetting the liver [bilem]’, the seat of the bile, can be appreciated in the context of a passage from Aretaeus of Cappadocia (1st–2nd century CE) regarding treatment of cholera (Adams, 1856):

“But if all the remains of the food have been discharged downwards, and if bile be evacuated, and if there still be bilious vomiting, retchings, and nausea, uneasiness and loss of strength, we must give two or three cupfuls (cyathi) of cold water, as an astringent of the belly, to stop the reflux, and in order to cool the burning stomach; and this is to be repeatedly done when what even has been drunk is vomited.”

The descriptions of the development of seasickness in monographs from the latter half of the 19th and early 20th centuries (Beard, 1881;

¹ Classical references to nausea were obtained from classical medical texts used in earlier publications (e.g., Balaban and Jacob, 2001; Balaban, Erlén and Siderits (eds), *The Skilful Physician*, Harwood Academic 1997; Balaban, Erlén and Siderits (eds), *The Ladies' Dispensary*, Routledge: New York, 2003); from a keyword search of Perseus Project database (<http://www.perseus.tufts.edu/hopper/>), from bibliographic references cited by recent secondary sources in the humanities (e.g., Rolfe, 1904), reference works such as R.J. Cunliffe's *A Lexicon of the Homeric Dialect* (1963) and from citations in references obtained from key word search of *The Index-Catalogue of the Library of the Surgeon-General's Office* through the IndexCat database (<https://www.nlm.nih.gov/hmd/indexcat/>).

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