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This is an author's accepted manuscript of a journal article published in the Current Opinion in Neurology. The final definitive version is available online at:

https://doi.org/10.1097/WCO.0000000000001018

Motion sickness: current concepts and management

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Word count: 2,672

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Abstract

Purpose of the review: Motion sickness is an ancient phenomenon that affects many people. Nausea, vomiting, disorientation, sweating, fatigue, and headache are just few of the many signs and symptoms that are commonly experienced during an episode of motion sickness. In the present review, we will provide an overview of the current research trends and topics in the domain of motion sickness, including theoretical considerations, physiological and neural mechanisms, individual risk factors, treatment options, as well as recommendations for future research directions.

Recent findings: More recently, motion sickness has been in the focus of attention in the context of two global technological trends, namely automated vehicles and Virtual Reality (VR). Both technologies bear the potential to revolutionize our daily lives in many ways, however, motion sickness is considered a serious concern that threatens their success and acceptance. The majority of recent research on motion sickness focuses on one of these two areas.

Summary: Aside from medication (e.g., antimuscarinics, antihistamines), habituation remains the most effective non-pharmacological method to reduce motion sickness. A variety of novel techniques has been investigated with promising results, but an efficient method to reliably prevent or minimize motion sickness has yet to emerge.

Keywords: simulator sickness, virtual reality, automated vehicles, sex, age

Introduction

Motion sickness (MS) causes nausea and/or vomiting, stomach awareness and/or discomfort, increased autonomic activity (cold sweating, pallor, flushing, changes in body temperatures), arousal changes (drowsiness, yawning, lethargy, fatigue), dizziness, and or/headache. MS occurs in two contexts: during physical movement, for instance when travelling by car, ship, airplane, or any other mode of transportation, or in the absence of physical movement, for instance when playing video games or watching a movie. In the latter case, the sensation of apparent self-motion (so-called vection [1]) is primarily driven by the visual system and MS in this context is often referred to as visually induced motion sickness (VIMS[1]), causing additional oculomotor issues such as eyestrain and eye discomfort. Note that vertigo and dizziness are motion sickness/VIMS symptoms that can also occur as part of vestibular disorders as outlined by the International Classification of Vestibular Disorders (ICVD). However, despite their similarities, motion sickness/VIMS should be viewed as syndromes that may include symptoms of visually induced vertigo and/or visually induced dizziness, but have different characteristics such as temporal profiles (e.g., gradual onset) and a more complex symptomatology compared to visually induced vertigo/dizziness (see [2●●] for details). MS/VIMS can show as a single episode or manifest itself as a disorder, with symptoms being consistently triggered by the same situations, severity not decreasing with repeated exposure, and leading to changes in one's behaviour and emotional responses (e.g., activity modifications, avoidance of motion stimuli) [2••].

[1] Note that depending on the visual device/technology used, other terms such as virtual reality induced symptoms and effects (VRISE), cybersickness, VR-sickness, Cinerama sickness, gaming sickness, or simulator sickness have been used in the literature. Here, we are summarizing these sub-types of motion sickness as VIMS.

Two current trends make motion sickness a topical issue: First, the era of automated vehicles has begun and it is expected that fully automated vehicles will eventually be on our roads. However, the risk of MS is significantly increased in automated vehicles, as the motion of the vehicle can no longer be controlled [3,4]. While drivers are far less affected, about 46% of the adult population experience MS as passengers in cars, making it a serious concern for the development of automated vehicles [5••]. Second, Virtual Reality (VR) has become mainstream and is a highly beneficial tool for rehabilitation, research, education, and training purposes. Unfortunately, VR users often experience VIMS [6••,7]. Reported incidence rates and severity are very variable but premature termination rates of VR sessions can be as high as 60% [8]. Consequently, MS/VIMS may jeopardize the success and the acceptance of these novel technologies. The majority of recent MS/VIMS research has been conducted with these topics in mind.

Theoretical considerations and related phenomena

According to the sensory conflict theory, a mismatch between the information delivered by the visual, vestibular, and/or somatosensory system that is not in accordance with the movement predicted by a cortical, internal model is the primary cause for motion sickness [2••]. In contrast, the postural instability theory claims that changes in one's ability to control posture and balance are the primary cause for motion sickness, preceding the onset of symptoms [9,10]. The latter theory has generated controversy since well controlled studies failed to find a relationship between postural control and motion sickness [11•].

MS/VIMS share a similar symptomatology with other medical conditions from which they need to be separated. For instance, dizziness and/or disorientation are commonly experienced during MS/VIMS, but vertigo in the absence of physical or apparent self-motion caused by normal head movements is not a symptom associated with MS/VIMS and suggests the involvement of vestibular dysfunction. Similarly, vertigo that is easily elicited by visual motion of objects (e.g., traffic, flashing lights) and not due to self-motion, can be due to vestibular disturbance (e.g., vestibular neuritis, Meniere's disease, benign paroxysmal positional vertigo [BPPV]) and often labelled as "visual vertigo" [12••]. Further, patients suffering from migraine or vestibular migraine have an increased risk of experiencing motion sickness [13], but headaches experienced as a consequence of MS/VIMS are not necessarily part of migraine. Lastly, the continuous sensation of body oscillation such as swaying or bobbing that persist after termination of provocative motion (e.g., when returning from a sea voyage to land) and can be accompanied by MS-like symptoms is considered Mal de Debarquement syndrome [14]

Neural and physiological basis

Fully functioning vestibular organs with intact semicircular canals and otoliths are a prerequisite for experiencing MS/VIMS. On a cortical level, the velocity storage integrator with activity in the vestibular-only neurons in the medial and superior vestibular nuclei as well as the role of the nodulus have been identified as crucial elements in the development of MS [15•,16]. Additionally, a complex interplay of motor and visceral efferent and afferent circuits involving brainstem areas such as the nucleus tractus solitarius, the dorsolateral reticular formation of the caudal medulla, and the parabrachial nucleus, the vagus nerve and spinal cord neurons, and the anterior cingulate cortex with input from the amygdala are known to be involved in the processes of nausea and vomiting [17,18].

The autonomic responses during MS/VIMS vary widely between individuals and a consistent pattern of physiological changes on a population level has not yet been identified [19•]. Historically, changes in stomach activity, electrodermal activity, and thermoregulation have been linked to MS/VIMS [2••]. There have also been indications that cardiovascular activity

[20] and respiration [21] may alter for participants that experience MS compared to non-sick participants. However, a coherent picture of autonomic responses for MS and VIMS has yet to emerge. More recently, studies applying deep learning and machine learning techniques in order to predict MS/VIMS based on physiological measures has gained more popularity [22•]. Recenti et al. [23] combined Electroencephalography (EEG) with postural measures to successfully classify their participants post-hoc as sick or non-sick. Similarly, Liao et al. [24] found good classification results when using EEG measures, but none of these studies was able to estimate the severity of MS/VIMS or to detect the onset of symptoms in real-time.

Influencing factors and individual susceptibility

Age and sex/gender

Age and biological sex have been identified as two of the most prominent factors determining the susceptibility to MS/VIMS. For MS, an inverted U-shaped relationship between age and MS susceptibility was found. MS in infants younger than 12 months is rare and susceptibility peaks in children 6-9 years of age, with a decrease MS susceptibility during adolescence and adulthood [5••,25••,26•]. However, in the context of VIMS, the role of age is less clear. Recordings from 4-10 years old children playing a VR-based video game suggested that they were only minimally affected by VIMS and only 2 out of 50 child participants asked to stop the gaming session due to mild discomfort [9]. Similar to MS, the likelihood of VIMS seems higher in adults younger than 35 years of age compared to those older than 35 years [8••]. By contrast, it has been suggested that VIMS susceptibility may increase towards the later stages of life, with older adults (age 65 or higher) being at elevated risk of experiencing VIMS [2••]. The distribution of VIMS susceptibility across the life-span remains somewhat inconclusive, highlighting the need for further research in this domain.

With regards to biological sex, it has been repeatedly reported that females experience MS and VIMS more frequently and more severely than men, both in self-reported surveys [5••,27,28] as well as in laboratory studies [29•,30]. However, it is noteworthy that some experimental studies failed to find differences in MS/VIMS between females and males [4,31], questioning the robustness of this effect. The reason for a potential sex-related difference in MS/VIMS susceptibility remains speculative. The severity of VIMS has been linked to the menstruation cycle in women, suggesting an involvement of the endocrine system [2••]. Alternatively, Stanney et al. [30] identified the inability to adjust the interpupillary distance in VR headsets as the primary reason for sex-related differences found in their study. Lastly, it has been speculated that the sex-related differences might be related to gender roles and stereotypes, with individuals identifying as feminine being more open to report MS/VIMS compared to individuals who identify as more masculine, but scientific evidence for this claim is missing. Moreover, increased susceptibility in females vs. males is likely to be objective and not subjective reporting bias since surveys of passengers at sea indicate a 5:3 female to male risk ratio for vomiting [12••].

Other individual risk factors

The likelihood of experiencing MS is strongly determined by an individual's history of MS [32]. The Motion Sickness Susceptibility Questionnaire (MSSQ) is arguably the most prominent tool to estimate MS susceptibility and is based on the frequency of MS as a child or during adulthood (e.g., in a car, bus, train etc.) and has been shown to reliably estimate MS susceptibility [26•,33]. A recent study with more than 239 ship passengers showed that MS susceptibility as measured by the MSSQ was the best predictor of MS experienced during the sea voyage [26•]. In addition to the MSSQ, the Visually Induced Motion Sickness Questionnaire

(VIMSSQ) [34•] was recently introduced to estimate VIMS susceptibility when using visual devices such as smartphones, VR, or simulators. Both the long version as well as the short version of the VIMSSQ [35] have shown promising results in first validation studies and explained more than 40% of variance in the observed VIMS data.

Individuals with a history of migraine or vestibular migraine are at a higher risk of experiencing MS/VIMS as these concepts have been closely linked to each other [13]. A study by Wurthmann et al. [36] exposed patients with vestibular migraine and healthy controls to a rotary chair test and found that those with vestibular migraine reported more severe MS and recovered slower from these symptoms than healthy participants. Further, trait anxiety has been shown to alter the course of MS during a flight simulator study [37], whereas other personality factors such as neuroticism have not been identified as relevant factors for MS/VIMS susceptibility [31]. Similarly, trait anxiety/neuroticsm failed as a significant predictor for MS/VIMS in another study [35] and also failed to predict sickness at sea [26•]. However, state anxiety showed strong relationships with MS during exposure to motion at sea, although this might equally have been a consequence of MS rather than an aggravating risk factor [26•].

Risk factors specific to MS in automated vehicles and VR

In addition to the general risk factors, the occurrence of MS in automated cars is also linked to the characteristics of the provocative motion. Historically, low-frequent motion at 0.2Hz has been identified as the most provocative motion profile with higher amplitudes resulting in more MS. More recent work delivered supporting evidence for this assumption, but also suggested that most provocative frequency range may vary between individuals, with some humans being more affected by motion around 0.4Hz [38]. Further, the passenger’s seating arrangement inside the vehicle affects the severity and likelihood of MS, with rear facing positions causing more MS than forward facing and sitting in the backseat being more provocative than sitting in the front row [5••]. Providing passengers with a view of the outside of the vehicle helps to anticipate the upcoming motion of the vehicle and significantly reduces MS [3,38,39]), although severe episodes of MS can also occur despite a clear view of the road ahead [5••].

VR technologies have continuously improved over the last years, addressing several concerns such as ergonomic comfort, increased time-lags for coupled head and visual motion, small field-of-views, or poor screen resolution. However, VIMS is still a concern for todays VR systems, mainly due to the nature of the content and/or user-related factors. A recent meta-analysis [8••] with 55 studies revealed three main factors affecting the likelihood of VIMS in VR users. First, VR games caused significantly more VIMS than static 360° videos or minimalistic scenes, showing that the type of VR content matters. Second, VR scenes with more visual information (i.e., content with fast visual changes) provoked more VIMS than scenes with less visual information. Lastly, the type of locomotion used to navigate through the virtual environment is crucial for VIMS, with actual walking resulting in lower VIMS than controller-based locomotion or static scenes (no visual or physical motion of the user or scene).

Pharmacological and non-pharmacological treatment options

Drugs used against MS can be divided into the following categories: antimuscarinics (e.g., scopolamine), H_1 anti-histamines (e.g., dimenhydrinate), and sympathomimetics (e.g., amphetamine). Other types of antiemetics are not effective against MS, including D_2 dopamine receptor antagonists, and $5HT_3$ antagonists used for side-effects of chemotherapy. This is probably because their sites of action are at vagal afferent receptors or the chemoreceptor trigger zone (CTZ) in the brainstem, whereas anti-MS drugs act at the vestibular brainstem-cerebellar areas [12••]. Antihistamines such as meclizine block the histaminergic receptors in the medulla, inhibiting the reception of histamine-based signals from the nucleus solitarius and the vestibular nuclei and are effective in counteracting MS [40,41]. Scopolamine, a muscarinic cholinergic blocker, has been shown to be effective against MS and can be used as transdermal patch or intranasally [42,43]. Scopolamine is an unselective blocker at all five muscarinic receptors M1 to M5. Recent evidence indicates that its anti-MS action is at central M5 receptors, whereas many of the unwanted side-effects are caused by actions at receptors M1-M4. Consequently, a future selective antagonist at M5 would produce good anti-motion sickness prophylaxis with very low side-effects [12••]. In a recent study, tradipitant, a NK1 antagonist, has been shown to successfully reduce vomiting in boat passengers during rough sea rides, but the reduction of other symptoms of motion sickness such as nausea was either non significant or very limited [44]. This is consistent with previous laboratory studies which have consistently failed to show effectiveness of NK1 antagonists against motion induced nausea in human [12••]. However, like most medications, anti-motion sickness drugs can have unwanted side-effects such as fatigue or drowsiness and pose a risk of abuse.

To date, the most effective non-pharmacological countermeasure against motion sickness and VIMS is habituation, with repeated exposure to the same provocative motion resulting in reduced motion sickness over time [26•,28]. However, full habituation can be time-consuming and unpleasant for the user, making it not the most practical solution. Other methods to reduce MS/VIMS have been tested over the past years, some of them showing promising results. For instance, galvanic vestibular stimulation (GVS) reduced VIMS in VR [45], specifically when combined with sounds or tactile stimulation [46•,47]. The positive effect of multisensory stimulation on VIMS has been shown for combinations of seat vibration and sounds that match the visual scene in a driving simulator [48], although the robustness of this multisensory effect remains questionable [49]. In addition, providing participants that were exposed to a VIMS-inducing stimulus with their favorite music reduced VIMS by 50%, irrespective of the music's level of arousal or valence [50]. Other methods that were found to reduce VIMS in VR included blurring of scene [51,52] or reducing the central field-of-view [53] when users navigate through VR, adding a stable, horizontally aligned visual reference [54], training visuo-spatial abilities [55], or using acupressure [56]. Despite these promising results, none of the current countermeasures can fully prevent or minimize MS and VIMS in everyone, making further investigations highly desirable.

Conclusion

Motion sickness (MS) and VIMS threaten the well-being and comfort of many people. Specifically, the increasing reliance on visual displays and devices in our daily lives (smartphones, tablets, VR, etc.) and the advent of automated vehicles make MS and VIMS timely and highly relevant topics, posing substantial hurdles that need to be overcome in order to take full advantage of these technologies. Thus, two major goals remain for the next decade. First, the development of simple, reliable non-pharmacological solutions that can prevent MS/VIMS is crucial. Recent approaches such as multisensory stimulation (e.g., vibration, auditory, GVS, etc), promoting a pleasant ambience via music or airflow, or optimizing habituation protocols delivered enticing results and could serve as the basis for future research endeavours. Second, it is important to reliable and accurately identify the onset of motion sickness and VIMS as early as possible in order to initiate appropriate countermeasures. To date, an objective measure of motion sickness and VIMS has yet to emerge, although the combination of physiological (e.g., Electroencephalography), behavioural (e.g., sway, eye movements), and machine/deep learning techniques has shown a promising start to get closer to this goal. Our understanding of motion sickness and VIMS has substantially increased over the past years, but there is still plenty left to discover.

Key points

- Motion sickness is a serious concern in the context of fully automated vehicles and Virtual Reality technologies.
- An individual's susceptibility to motion sickness is determined by a variety of risk factors including age and sex.
- Machine learning techniques have been introduced to detect/predict motion sickness on the basis of physiological signals.
- Habituation remains the most effective method to reduce motion sickness, with several novel countermeasures being investigated.

Acknowledgements

Acknowledgements: none.

Financial support and sponsorship: none.

Conflict of interest: none.

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