Title

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Journal

Otology & Neurotology, 41(8)

ISSN

1531-7129

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Publication Date

2020-09-01

DOI

10.1097/mao.0000000000002705

Peer reviewed

HHS Public Access

Author manuscript

Otol Neurotol. Author manuscript; available in PMC 2021 September 01.

Published in final edited form as:

Otol Neurotol. 2020 September ; 41(8): 1116–1121. doi:10.1097/MAO.0000000000002705.

The Relationship between Vestibular Migraine and Motion Sickness Susceptibility

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Abstract

Objectives: To determine the relationship between vestibular migraine (VM) and motion sickness (MoS) susceptibility and their comorbidity in a large student population, and to assess whether experiencing MoS is associated with higher susceptibility for VM.

Methods: Surveys including Motion Sickness Susceptibility Questionnaire (MSSQ) and questions assessing migraine-related symptoms as well as family history of motion sickness and migraine headache were distributed to the university undergraduate students through Facebook and email. Diagnosis of definite VM (dVM) was based on the criteria of the International Classification of Headache Disorders.

Results: Of 277 survey responders, 148 (53%) were found to be susceptible to MoS in which 74 (50%) met the criteria for dVM. Only childhood MSSQ score was significantly higher in participants with dVM compared to those without dVM (25.78 ± 15.89 *vs.* 20.77 ± 14.28, $p = 0.04$); however, its significance faded out by regression analysis. Multivariate logistic regression showed having 1st degree relative with migraine headache ($p = 0.02$), neck stiffness ($p = 0.001$), and sinus pain, facial pressure or headache with wind exposure ($p = 0.02$) to be independently associated with presence of dVM in MoS subjects.

Conclusions: Though participants with MoS and dVM had significantly greater rates of migraine-related symptoms and family history of migraine headache compared to those with MoS only, childhood and adulthood MSSQ scores were similar. This and the high prevalence of dVM in our MoS cohort may suggest an existing association between MoS susceptibility and VM.

Keywords

Vestibular migraine; Motion sickness; Migraine-related symptom; Migraine; Family history

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Conflicts of Interest: None

Introduction

Motion sickness (MoS) refers to the autonomic response of nausea, vomiting, pallor, cold sweating, and other signs and symptoms provoked by a variety of motion environments or stimuli (1). The etiology and mechanism of MoS are not clear; however, there are various theories that have been proposed. The sensory conflict theory is the most widely accepted, which proposes that MoS is due to an intersensory mismatch involving conflicting vestibular, visual, and somatosensory stimuli (2,3). In order to sense motion and body position and to maintain gaze during head and body movements, the brain relies on sensory input from the labyrinthine vestibular system (4). The vestibular system serves as an effective sensor of disequilibrium and those with functioning vestibular organs will not normally experience MoS (3,5).

Previous studies have found that MoS is more prevalent in patients with migraine (30% −70%) than in headache-free patients or those with tension headaches (20%−40%) (6–11). A genetic database review by Hromatka *et al.* determined that a single nucleotide polymorphism (SNP) of PRDM16 was significantly associated with both MoS and migraine suggesting similar etiology, but it was unable to determine if the SNP was causal of the phenotypes (5). In migraine, headache frequently coexists with symptoms of vestibular dysfunction, including MoS, vertigo, and gait instability. When patients experience episodes of vestibular symptoms in conjunction with migraine headache or migraine-related features, they may have a condition known as vestibular migraine (VM) (12). Jeong *et al.* found that those with MoS have higher susceptibility to VM than to migraine headache in general, suggesting a link between MoS and VM (8). This survey-based study aims to relate the two phenotypes (i.e., MoS and VM) and further determine their comorbidity in a large undergraduate student population. This may help reveal an association between the two conditions and the potential for utilizing a common course of treatment and management.

Methods

With institutional review board approval, a survey study was conducted over the span of eight months from October 2017 to May 2018. The survey was electronically distributed through Facebook (Facebook Inc., Menlo Park, California) and emailed to our university's undergraduate students. The survey was administered through RedCap (Vanderbilt, Nashville, Tennessee) (13). Twenty participants were incentivized via $25 Amazon gift card raffle upon completion of the survey. The survey included self-reported demographical information, the revised Motion Sickness Susceptibility Questionnaire (MSSQ), family history of motion sickness and migraine headache, and presence of migraine related symptoms, as shown in supplemental digital content 1. Subjects were classified as having MoS if they responded "yes" to the question "Do you experience motion sickness?".

MSSQ scores were calculated based on the revised and simplified hand-scoring method, where MSSQ-A and MSSQ-B represent motion sickness susceptibility in childhood and in the past 10 years, respectively (14). MSSQ-A was calculated using the following formula as described by *Golding et al.*: MSSQ-A= [2.64 × (total sickness score as a child)] × [9 / (number of types of transportation as a child)] (14). Sickness scores were based on the

severity of nausea and vomiting symptoms (ranging 0–4) for each mode of transportation. MSSQ-B scores were also calculated with the same formula but used adult sickness scores and modes of transportations experienced as an adult instead. The MSSQ total score is the sum of the MSSQ-A and MSSQ-B scores.

Participants were specifically evaluated for meeting the International Classification of Headache Disorders (ICHD) 3rd edition beta criteria for dVM published by the International Headache Society (IHS) as shown in Table 1 (9). Demographics, prevalence of migraine-related symptoms, and MSSQ scores were compared between those with and without dVM. Univariate analysis including the chi-square or Fisher's exact tests and independent sample *t*-test were performed to compare the categorical and numerical variables between the groups, respectively. Variables whose relationship reached the cut-off *p* value of 0.05 were extracted for second-step analysis. Accordingly, these variables were included in the multivariate binary logistic regression, were their independent effects as well as adjusted odds ratios were determined. SPSS 17.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Throughout the analysis, $p < 0.05$ was considered statistically significant.

Results

Of 277 responders to the survey, 148 (53%) participants who experienced MoS were included for further analyses (Table 2). Seventy-four (50%) of these participants met the criteria for dVM, *vs.* 30 (23%) of patients without MoS ($p < 0.001$). Participants with dVM were younger than those without dVM (20.24 ± 1.94 *vs.* 21.57 ± 4.83 years, $p = 0.03$). The MSSQ-A, MSSQ-B, and MSSQ total scores in participants with dVM were 25.78 ± 15.89, 15.20 ± 11.76, and 40.98 ± 24.09, respectively. Only childhood MSSQ score (MSSQ-A) was significantly higher in participants with dVM compared to those without dVM (25.78 ± 15.89 *vs.* 20.77 ± 14.28, $p = 0.04$). Of those with dVM, 46% reported a 1st degree relative with migraine headache, compared to 20% of those without dVM ($p = 0.002$).

Compared to those without dVM, participants with dVM reported significantly more migraine-related symptoms such as visual motion sensitivity (69% *vs.* 50%, $p = 0.03$), head motion sensitivity (31% *vs.* 7%, $p < 0.001$), and sinus pain (subjective pain over the frontal or maxillary sinuses), facial pressure, or headache when exposed to wind or air conditioning (55% *vs.* 27%, $p = 0.001$), which help confirm our methodology of appointing dVM diagnoses based on survey responses. Additionally, the prevalence of light sensitivity (38% *vs.* 19%, $p = 0.01$), weather change sensitivity (31% *vs.* 15%, $p = 0.03$), neck stiffness (70% *vs.* 42%, $p = 0.001$), history of recurrent migraine headaches (35% *vs.* 17%, $p = 0.02$), history of allodynia of scalp or face (16% *vs.* 4%, $p = 0.02$), and mental confusion/head fog (72% *vs.* 45%, $p = 0.001$) were significantly higher in participants with dVM compared to those without dVM (Table 3).

Multivariate binary logistic regression was performed on variables with significant *p* values in the previous step to determine the independent association of each factor with dVM (Table 4). In survey responders with MoS, having a 1st degree relative with migraine headache was independently associated with higher chance of dVM ($p = 0.02$, OR = 3.02,

95% CI = 1.21–7.58). Furthermore, neck stiffness ($p = 0.001$, OR = 4.17, 95% CI = 1.73–10.03) and sinus pain, facial pressure, or headache with wind exposure ($p = 0.02$, OR = 2.64, 95% CI = 1.13–6.11) were two migraine-related symptoms found to be predisposing factors for dVM in subjects with MoS.

Discussion

A potential association between motion sickness and vestibular migraine

We found that the prevalence of dVM in a random population of individuals with motion sickness is 50%. This is much higher than the approximate prevalence of migraine and vertigo in 16% and 7% of the general population, respectively, with the comorbidity occurring in rates slightly higher than 3% (15). This discrepancy suggests the presence of a relationship between MoS and VM, suggesting that people with MoS may be more likely to have co-morbid VM compared to the general population. The susceptibility of MoS in VM patients has been studied (16); however, the prevalence of dVM in those with MoS is yet unclear. We found that half of participants with MoS also suffered from dVM in which the adulthood and total MSSQ scores were not significantly different than those without dVM. Although the childhood MSSQ score initially appeared statistically different between the two groups, after analysis with multivariate linear regression, which is used to analyze the relationship between an outcome and a possible explanatory variable while controlling for other explanatory variables (17), the difference disappeared, meaning that childhood MSSQ scores were ultimately similar between both groups. Participants with dVM had a higher probability of having a 1st degree relative with migraine headache (46%) compared to those without dVM (20%). In our study, participants with dVM showed higher prevalence of some migraine-related symptoms than those without dVM (Table 3), two of which were independently associated with meeting dVM criteria via regression analysis.

Though VM affects more than one percent of the general population (15), in our study of undergraduate students with self-perceived MoS, 50% were found to have dVM, suggesting a predisposition to VM in those with MoS. Sharon and Hullar have demonstrated the reverse relationship by reporting elevated MoS and MSSQ scores in VM patients compared to controls (16). Within our MoS cohort, those with dVM did not have different self-perceived degrees of MoS susceptibility and had similar MSSQ-B and MSSQ total scores, compared to those without dVM. Furthermore, MSSQ-A score which was initially significantly different between the two groups became non-significant after regression analysis to factor in various potential confounders. Though this finding neither confirms nor contradicts the validity of the MSSQ scoring since both groups were subjects with MoS, it further demonstrates a lack of a true association between MSSQ scores and meeting dVM criteria. This might be due to other more important underlying pathophysiologies of VM, or it could be due to dVM criteria being too strict to include all susceptible patients.

According to Boldingh *et al.* in their study of 99 patients undergoing vestibular evoked myogenic potential (VEMP) testing, patients with VM were found to be more sensitive to motion triggers and reported more MoS than other migraineurs (18). In an epidemiologic report of 749 patients with vertigo or dizziness, Strupp *et al.* found that MoS is a relevant comorbidity of most vestibular disorders, including VM (2). In comparison, Murdin *et al.*

found a significant increase in MSSQ scores in those with VM following rotation and tilt in a motorized chair, however the increase was not different than the general migraine group (9). In addition, patients with bilateral vestibulopathy had reduced MSSQ scores, suggesting that the vestibular system and sensory mismatch play a role in the mechanism of MoS. However, in their study, some individuals with VM reported reductions in susceptibility as well, suggesting heterogeneity in the underlying pathomechanism of VM and MoS (9).

Interestingly, there was no significant difference in those with MoS who met criteria for migraine headache both with dVM and without dVM (Table 2). This is potentially because there exists a large group of migraine headache sufferers who experience vertigo, light and sound sensitivity, MoS, and other migraine-related symptoms but who do not meet the strict criteria of experiencing vertigo and migraine headache simultaneously (19). If MoS, VM, and migraine headache are indeed associated, then it is not too surprising that a similar proportion of those with dVM and those without dVM experience migraine headache when both groups also experience MoS.

The relationship between head motion sensitivity, motion sickness, and vestibular migraine

Motion sickness can be provoked or worsened by active head movements in the presence of vestibular motion (experienced in a car, bus, train, or plane) and by visually induced simulation (experienced with video games on large screens, three dimensional movies, and virtual reality) (3,20,21). Vection, or the sensory-spatial illusion that creates false sensations of self-motion, has been found to be correlated with levels of visually induced MoS and postural status (22). Lewis *et al.* found a large reduction in perceptual motion thresholds in VM patients compared to control and migraine subjects, when subjects were roll tilted at a frequency of 0.1 Hz (23). Their finding suggests an abnormality in the perception of head motion which appears to be derived from changes in semicircular canal-otolith integration in the brain. It is known that head and visual motion can induce MoS; however, our study suggests that MoS subjects who are sensitive to head and visual motions may also have greater susceptibility to meeting IHS dVM criteria. Further studies are needed to understand this interaction and diagnostic sensitivity.

Common environmental sensitivities may make identifying vestibular migraine in those with motion sickness difficult

In our study, rates of dVM were significantly higher in MoS subjects experiencing environmental sensitivities (e.g., changes in weather or light), which are known triggers for VM and migraine (24). However, these environmental factors were not independently associated with dVM prevalence via multivariate logistic regression. There is evidence that migraine symptoms are associated with the brain's central neuronal hyperexcitability (25), and those with migraine headaches are more likely to experience discomfort from bright light, loud sounds, smells, and motion as well as many other sensory inputs that are not disturbing to non-migraineurs (26). The weather-related triggers involve changes in weather and include storm fronts, such as rapid changes in barometric pressure, and changes in season (26). Neuhauser *et al.* reports that the most common vestibular symptoms in vestibular migraineurs are rotational vertigo, followed by intolerance of head motion, and

positional vertigo (27). In addition, visual motion and MoS were also common symptoms. The lack of clear association between some migraine-related symptoms and presence of dVM in our study may present a new challenge in characterizing dVM in MoS population, warranting further investigations into their pathophysiologic differences.

Triptans as a possible treatment for motion sickness in individuals with vestibular migraine

Due to a lack of criteria for diagnosis of VM prior to ICHD-3, and subsequent lack of data to support optimal pharmacological agents for VM, current treatment recommendations for VM are largely based on expert opinions and observational or retrospective studies rather than randomized placebo-controlled trials (28). To our knowledge, there exist only three randomized placebo-controlled studies that address the treatment of VM. Neuhauser *et al.* found an acute improvement of vertigo symptoms (rotational vertigo, other illusory self or object motion, positional vertigo, or head motion intolerance) at two hours in eight patients treated with zolmitriptan compared to placebo (29). In addition, in their two clinical trials of ten and twenty-five adults with migraine with and without vertigo, Furman *et al.* found that rizatriptan prevented the development of MoS and severity of MoS symptoms in patients with VM (30). Interestingly, rizatriptan did not affect MoS in migraineurs without vertigo. Based on these studies, there is a potential for triptan drugs to prevent or treat MoS in the VM population. There is a need for further clinical trials to assess the efficacy of treatments for the comorbidity of VM and MoS. In addition, drugs to treat MoS or VM independently should be studied to treat either condition.

In terms of migraine medication use, a low percentage of patients in our study utilized migraine medications (12.2% in participants with dVM *vs.* 4.0% in those without dVM). This may be because active migraine headaches are not necessary in order to meet criteria for either dVM or MoS, therefore these patients would not be using migraine medications at the time of answering the survey. Furthermore, about 30% of patients who do have migraine headaches do not see a physician for them and may self-treat with non-migraine medications or therapies, with an additional 20% having seen a physician in the past but not any time within the last year (31). This may present a challenge in accessing the almost 50% of the migraine patient population that experiences migraine headache, VM, or migraine-related symptoms but does not see a physician for them. This is particularly true for sufferers who experience symptoms that are not classically associated with migraine, such as vertigo.

Limitations of our study

Further large, multi-institutional studies are needed to allow for accurate and generalizable reporting of the prevalence of VM and migraine-related symptoms in the population of those who experience MoS. There are several limitations in this study. The survey-based nature makes answers susceptible to recall bias especially regarding childhood experiences. Furthermore, knowledge of family history for MoS and migraine may be limited. Even if family history is known, it may be biased towards a negative history, as it would require self-observation or reporting by other family members. Our incorporation of incentivizing prizes (entrance into a raffle for a $25 Amazon gift card) to promote survey participation may lead to exaggerated values or false positive reports from a minority of participants. In addition,

subjects with MoS and VM symptoms may have been more inclined to respond to this survey due to its online nature which would explain our high incidence of MoS (53%) in our population compared to other studies (32). In particular, the use of Facebook as a means to distribute the survey may bias the responses toward the demographics of the platform itself, and it is possible that even other online social media sites could produce a different profile of responses. Lastly, our appointment of dVM diagnosis based on the IHS criteria was limited to questionnaire responses and short of real-life clinical scenarios where additional physical exams and diagnostic tests are utilized to rule out other diagnoses.

Conclusion

Half of our participants with MoS also suffered from dVM. The MSSQ scores were not significantly different between subjects meeting or not meeting dVM criteria. However, participants with dVM had a greater propensity of experiencing some migraine-related symptoms and reported higher rates of family history with migraine headache. These findings may suggest an existing association between MoS susceptibility and VM, warranting further studies to investigate distinguishing pathophysiologic features and whether similar treatment strategies can be efficacious in both conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Financial Disclosure: Mehdi Abouzari is supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant TL1TR001415-05.

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Table 1.

The International Classification of Headache Disorders (ICHD) 3rd edition beta criteria for vestibular migraine

Diagnostic criteria of definite vestibular migraine:
A. At least five episodes fulfilling criteria C and D
B. A current or past history of migraine without aura or migraine with aura
C. Vestibular symptoms of moderate or severe intensity, lasting between 5 minutes and 72 hours
D. At least 50% of episodes are associated with at least one of the following three migrainous features:
1. headache with at least two of the following four characteristics:
a) unilateral location
b) pulsating quality
c) moderate or severe intensity
d) aggravation by routine physical activity
2. photophobia and phonophobia
3. visual aura
E. Not better accounted for by another ICHD-3 diagnosis or by another vestibular disorder.
Diagnostic criteria of probable vestibular migraine:
A. At least five episodes with vestibular symptoms of moderate or severe intensity, lasting between 5 minutes and 72 hours
B. Only one of the criteria B and C for vestibular migraine is fulfilled (migraine history or migraine features during the episode)
C. Not better accounted for by another vestibular or ICHD diagnosis

Table 2.

Demographics, MSSQ scores, migraine prevalence, and family history of survey responders with motion sickness

Characteristic	Subjects with dVM (n=74)	Subjects without dVM (n=74)	Total (n=148)	*p* value
Female (%)	58 (78.4)	58 (78.4)	116 (78.4)	1.00
Age (mean ± SD)	20.24±1.94	21.57±4.83	20.90±3.38	0.03*
Self-perceived MoS susceptibility (%)				1.00
Slightly	31 (41.9)	35 (47.3)	66 (44.6)	
Moderately	27 (36.5)	24 (32.4)	51 (34.4)	
Very much so	16 (21.6)	15 (20.3)	31 (20.9)	
MSSQ scores				
MSSQ-A	25.78±15.89	20.77±14.28	23.27±15.26	0.04*
MSSQ-B	15.20±11.76	13.43±12.69	14.31±12.23	0.38
MSSQ total	40.98±24.09	34.19±22.63	37.59±23.54	0.08
Fulfill ICHD criteria for migraine headache (%)	25 (33.7)	20 (27.0)	45 (30.4)	0.37
Family history (%)				
1st degree relative with MoS	58 (78.4)	52 (70.3)	110 (74.3)	0.43
1st degree relative with migraine headache	34 (46.0)	15 (20.3)	49 (33.1)	0.002*

MSSQ: Motion Sickness Susceptibility Questionnaire; dVM: definite vestibular migraine; MoS: motion sickness; MSSQ-A: MSSQ score in childhood; MSSQ-B: MSSQ score in the past 10 years; ICHD: The International Classification of Headache Disorders; SD: standard deviation; Asterisk denotes to significant *p* value.

Table 3.

Prevalence of migraine-related symptoms in survey responders with motion sickness

Symptom	Subjects with dVM (n=74)	Subjects without dVM (n=74)	Total (n=148)	*p* value
Visual motion sensitivity	51 (69.0%)	37 (50.0%)	88 (59.4%)	0.03*
Head motion sensitivity	23 (31.1%)	5 (6.7%)	28 (19.0%)	< 0.001*
Sinus pain, facial pressure, or headache when exposed to wind	41 (55.4%)	20 (27.0%)	61 (41.2%)	0.001*
Light sensitivity	28 (37.8%)	14 (19.0%)	42 (28.4%)	0.01*
Sound sensitivity	17 (23.0%)	11 (14.8%)	28 (19.0%)	0.29
Smell sensitivity	25 (33.8%)	14 (19.0%)	39 (26.3%)	0.06
Weather change sensitivity	23 (31.1%)	11 (14.8%)	34 (23.0%)	0.03*
Medication sensitivity	6 (8.1%)	2 (2.7%)	8 (5.4%)	0.27
Neck stiffness	52 (70.3%)	31 (41.9%)	83 (56.1%)	0.001*
History of recurrent migraine headaches	26 (35.1%)	13 (17.5%)	39 (26.3%)	0.02*
History of ice cream headaches (brain freeze)	63 (85.1%)	57 (77.0%)	120 (81.1%)	0.29
History of allodynia of scalp or face	12 (16.2%)	3 (4.0%)	15 (10.1%)	0.02*
Mental confusion (head fog)	53 (71.6%)	33 (44.6%)	86 (59.4%)	0.001*
History of migraine medication use	9 (12.2%)	3 (4.0%)	12 (8.1%)	0.13

dVM: definite vestibular migraine; Asterisk denotes to significant *p* value.

Table 4.

The results of multivariate analysis to evaluate the predisposing factors for dVM in survey responders with motion sickness

Factor	*p* value	Odds ratio (95% CI)
Age	0.16	0.87 (0.72–1.05)
MSSQ-A	0.12	1.02 (0.99–1.05)
1st degree relative with migraine headache	0.02*	3.02 (1.21–7.58)
Visual motion sensitivity	0.24	1.66 (0.71–3.86)
Head motion sensitivity	0.06	3.26 (0.92–11.49)
Sinus pain, facial pressure, or headache when exposed to wind	0.02*	2.64 (1.13–6.11)
Light sensitivity	0.69	1.21 (0.47–3.08)
Weather change sensitivity	0.48	1.44 (0.51–4.05)
Neck stiffness	0.001*	4.17 (1.73–10.03)
History of recurrent migraine headaches	0.22	1.81 (0.69–4.77)
History of allodynia of scalp or face	0.35	2.08 (0.44–9.80)
Mental confusion (head fog)	0.12	1.94 (0.83–4.54)

dVM: definite vestibular migraine; MSSQ-A: Motion Sickness Susceptibility Questionnaire score in childhood; CI: confidence interval; Asterisk denotes to significant *p* value.