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RESEARCH ARTICLE

A comparative study of cybersickness during exposure to virtual reality and "classic" motion sickness: are they different?

Alireza Mazloumi Gavgani,[1] Frederick R. Walker,[1] Deborah M. Hodgson,[2] and Eugene Nalivaiko[1]

[1]*School of Biomedical Sciences and Pharmacy, University of Newcastle, Callaghan, New South Wales, Australia; and* [2]*School of Psychology, University of Newcastle, Callaghan, New South Wales, Australia*

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Mazloumi Gavgani A, Walker FR, Hodgson DM, Nalivaiko E. A comparative study of cybersickness during exposure to virtual reality and "classic" motion sickness: are they different? *J Appl Physiol* 125: 1670–1680, 2018. First published October 4, 2018; doi:10.1152/japplphysiol.00338.2018.—Existing evidence suggests that cybersickness may be clinically different from "classic," motion-induced sickness; this evidence was, however, obtained in separate studies that focused on just one of the two conditions. Our aim was to bring clarity to this issue by directly comparing subjective symptoms and physiological effects of motion sickness induced by physical motion (Coriolis cross-coupling) and by immersion in virtual reality (ride on a roller coaster) in the same subjects. A cohort of 30 young, healthy volunteers was exposed to both stimulations in a counterbalanced order on 2 separate days ≥1 wk apart. Nausea scores were recorded during the exposure, and the Motion Sickness Assessment Questionnaire (MSAQ) was used to profile subjective symptoms postexperiment. Tonic and phasic forehead skin conductance level (SCL) was measured before and during exposure in both stimulation methods. We found that the nausea onset times were significantly correlated in both tests ($r = 0.40$, $P = 0.03$). Similarly, the maximum nausea ratings were significantly correlated during both provocations ($r = 0.58$, $P = 0.0012$). Symptom-profiling with the MSAQ revealed substantial and significant correlations between total symptom scores ($r = 0.69$, $P < 0.0001$) between each of 4 symptom clusters and between 15/18 individual symptoms assessed in both conditions. Both virtual reality and Coriolis cross-coupling provocations caused an increase in tonic SCL associated with nausea [mean difference (mean diff) = 5.1, confidence interval (CI) = (2.59, 6.97), $P = 0.007$ and mean diff = 1.49, CI = (0.47, 7.08), $P = 0.0001$, respectively], with a close correlation between the conditions ($r = 0.48$, $P = 0.04$). This was accompanied by a significant increase in the amplitude of phasic skin conductance transients in both visual stimulation and Coriolis cross-coupling when participants reported maximum nausea compared with no nausea [mean diff = 0.27, CI = (0.091, 0.63), $P < 0.001$ and mean diff = 0.235, CI = (0.053, 0.851), $P < 0.006$, respectively]. We conclude that symptoms and physiological changes occurring during cybersickness and classic motion sickness are quite similar, at least during advanced stages of these malaises.

NEW & NOTEWORTHY Expansion of virtual reality (VR) technology has provoked an interest in cybersickness, a subtype of motion sickness induced by immersion in VR. Finding means for preventing and managing cybersickness requires good understanding of its nature, including its relationship to "classic" motion sickness. The knowledge about this relationship is controversial, partly because there were no studies where the same cohort was exposed to the two provocations. With this approach, we demonstrate that symptoms and physiological manifestations of the two conditions are identical.

cybersickness; motion sickness; nausea; skin conductance; virtual reality

INTRODUCTION

Dominant symptoms of motions sickness (MS) are nausea and cold sweating. Careful clinical profiling has, however, revealed that MS has much broader, complex, and diverse symptomatology. Previous studies have categorized MS symptoms into four main clusters: gastrointestinal (stomach awareness, nausea, vomiting), central (fainting, lightheadedness, blurred vision, disorientation, dizziness, sensation of spinning), peripheral (sweating, feeling hot), and sopite (annoyance, drowsiness, tiredness, uneasiness; Ref. 11). The latter group of symptoms is less known; they may develop as a sole manifestation of MS or can be combined with other symptoms. Individual susceptibility to MS varies greatly and depends both on the scale of provocation and on individual factors such as sex, age, and ethnic background (15).

Neural mechanisms responsible for MS are still poorly understood. Currently, the dominating "sensory-mismatch" theory suggests that MS develops when conflicting signals are received from the spatial orientation senses: the vestibular system, the eyes, and the nonvestibular proprioceptors (2, 3, 38). This conflict can be initiated by purely vestibular stimuli (e.g., Coriolis cross-coupling leading to canal-otolith mismatch; Refs. 4, 13), by purely visual stimuli (e.g., optokinetic drum leading to visual-vestibular mismatch; Refs. 18, 25, 50), or by combination of the two (as it happens in most instances of car-, air-, and seasickness). Vision on its own is not essential for MS since blind people are susceptible to it (17). On the other hand, subjects with bilateral vestibular deficit are immune not only to motion-induced MS, but also to visually induced MS (19). In this case, visual stimuli serve as a trigger for MS, but the integrity of the vestibular system is essential for its development. Earlier studies (23, 29, 34, 46) have concluded that MS and nausea are associated with variations in brain activity (region-specific increases and decreases) in diverse regions such as the medial prefrontal cortex, the ventromedial prefrontal cortex/pregenual cingulate cortex, and the anterior insula and the midcingulate cortices related to the cognitive and sensory components of this syndrome (42).

Cybersickness is a subtype of motion sickness that may accompany immersion in virtual reality (VR). Although its first

Address for reprint requests and other correspondence: E. Nalivaiko, School of Biomedical Sciences and Pharmacy, Univ. of Newcastle, Callaghan, NSW 2308, Australia (e-mail: eugene.nalivaiko@newcastle.edu.au).

description was made decades ago (45), it is only recently that it gained the attention of academic researchers and industry developers. An explosion of consumer VR head-mounted displays (such as Oculus Rift, Samsung Gear VR, and HTC Vive) that occurred during the last several years was paralleled by dramatic increase in both mass media and research publications that confirmed the provocative liability of the technology (43, 44). According to the sensory-mismatch theory, the most likely cause of cybersickness is a mismatch between visual stimuli and the appropriate vestibular or proprioceptive feedback. Additional factors contributing to motion sickness can be separated into either hardware-dependent (sensor-induced delay, display flicker, frame rate) or content-dependent (visual flow direction, presence of linear or angular accelerations) categories (8, 27). Still another distinct subtype of MS is simulator sickness; the bulk of research on this subject was performed in flight simulators, where participants received both visual and, to various extents, motion stimuli. It was reported that rotary-wing simulators had more provocative effects compared with fixed-wing ones (22).

One unresolved issue in the field of MS research is whether different subtypes of MS represent separate clinical entities. The answer to this question could be obtained by comparing subjective symptoms and physiological changes induced by different MS-provoking stimuli, and few such comparisons were indeed performed. For example, Kennedy et al. (22) reported that seasickness and simulator sickness differ in their symptom profiles, with nausea being a dominant symptom for the former and oculomotor disturbances for the latter. In another publication (41) comparing several separate studies, the authors concluded that exposure to virtual environments can result in more severe symptoms than exposure to simulators, and although symptom profile differed between the two conditions, in neither case nausea was a dominant symptom. On the other hand, we found that the symptom profile of cybersickness was identical to that of "classic" motion-induced MS, with nausea having the highest score (10). This controversy motivated us to design and conduct the current study.

We propose and advocate the idea that to compare symptomatology of two (or more) related disorders, data should be collected from subjects who have progressed to a similar degree of malaise/severity. In many instances (e.g., respiratory viral infections), dominant symptoms during a prodromal stage are very different from dominant symptoms during disease culmination, and the same could be true for the group of MS disorders. We suggest that lack of control for this confounding factor might underlie the differences reported in the studies cited above. Another potential source of apparent differences is the interindividual variability in sensitivity to MS-inducing stimuli. For instance, in one of the studies where cybersickness was reported to provoke greater severity compared with simulator sickness, one of the limitations reported by the authors was the differences between their subjects (college students vs. military pilots in cybersickness and simulator sickness experiments, respectively; Ref. 41). With these considerations in mind, we aimed to compare symptom profiles of classic MS and cybersickness; to this end, we exposed our subjects to two well-validated provocative stimuli, Coriolis cross-coupling (4, 9, 13) for the former and a virtual ride on a roller coaster (10, 27) for the latter. To control for MS severity, we asked subjects to continue exposure until it became too uncomfortable to tolerate it. To exclude confounding effects of individual sensitivity, we used the same cohort of volunteers in both tests, in a counterbalanced manner. We also complemented subjective symptom scoring with a recording of forehead sweating, the most sensitive objective biomarker of MS (11, 12, 41).

An additional question that we intended to address in the current set of experiments is whether there is a correlation between the sensitivity to provocative motion and the sensitivity to provocative visual stimuli. If present, such dependence would allow using simple and relatively inexpensive VR technology for occupational preselection tests in those professions where motion sickness is an exclusion criterion or represents a common occupational hazard (e.g., pilots, drivers of public transport, crane operators, et cetera). It has been confirmed that those who score high on retrospective motion sickness susceptibility questionnaires are also more susceptible to provocative visual (6, 32) or vestibular intervention (26). However, to the best of our knowledge, so far there were no studies where sensitivity to provocative visual and vestibular stimulation was assessed in the same cohort, thus allowing direct comparison of the stimulation type. To this end, on different days, we subjected our volunteers to highly provocative VR or vestibular stimuli and compared their subjective symptoms and physiological responses to these stimuli. Our two working hypotheses were that *1*) both provocation methods will elicit similar symptom profiles and *2*) sensitivity to one type of provocation will correlate with sensitivity to the other.

METHODS

Study participants. The study was conducted on 30 healthy volunteers (16 women and 14 men) aged 25.8 ± 5.6 yr. The study protocol was approved by the Human Research Ethics Committee of the University of Newcastle. The volunteers were randomly allocated to two groups ($n = 15$ each); on 2 different days (≥1 wk apart), the first group experienced a virtual ride on a roller coaster, whereas participants of the alternative group experienced vestibular stimuli (rotating chair, RC). The study was designed in a counterbalanced manner so that participants from one group who experienced a virtual ride on the 1st experimental day experienced rotating chair on the 2nd day, whereas the order was opposite in the second group.

Experimental outline. On the day of arrival to the laboratory (air-conditioned room), after signing informed, written consent, subjects completed the Motion Sickness Susceptibility Questionnaire (MSSQ; Ref. 12) and the Motion Sickness Assessment Questionnaire (MSAQ; Ref. 11). The MSAQ was repeated after the test termination on each experiment day. In this questionnaire, a list of common MS symptoms was presented to the participant. The symptoms were categorized in four clusters: gastrointestinal (nausea, feeling sick in the stomach, feeling queasy, about to vomit), central (faintlike, lightheadedness, disoriented, dizzy, and spinning), peripheral (sweaty, hot, clammy, cold sweat, temperature discomfort, need for fresh air), and sopite (annoyed, drowsy, tired, and uneasy). When answering each question of the MSAQ, the participant assigns a value from a range of 0 ("not at all") to 8 (severe). These ratings were then summed for each group of related questions and used in a formula for each subscale, where rating = (sum of each subclass symptom rating)/[(number of the questions related to the corresponding subclass) × 8]. The overall MSAQ score was calculated as score = (sum of all items)/[(number of all questions) × 8]; this results in a value between 0 and 4.

Forehead skin conductance was measured before and during the experiment using a wireless EquiVital LifeMonitor (Hidalgo) with self-adhesive surface electrodes. The electrodes were placed on the right and left sides of the forehead 1 cm below the hairline, at about

the lateral corners of the eyes. The sensors were connected wirelessly by means of wireless-fidelity dongle to a computer running Chart 8.0 (ADInstruments, Sydney, Australia). To compute the phasic component of the skin conductance signal, we applied a digital high-pass filter with a cutoff frequency of 0.05 Hz (13, 14). The amplitude (root mean square) and frequency of skin conductance level (SCL) transients (phasic component) were calculated using LabChart software. A verbal rating of nausea was obtained from subjects every 30 s during the experiments. The nausea score ranged from 0 (no effect) to 9 (just about to vomit).

Motion sickness provocations. In the VR experiment, after fitting the head-mounted VR display (Oculus Rift DK1; Oculus VR), a 5-min baseline recording of forehead skin conductance was performed. During this period, a stereoscopic neutral static image was displayed on the rift monitor. Subsequently, the VR roller-coaster simulation (Helix; ArchiVision) was activated. The ride lasted for 15 min or until subjects felt uncomfortable and decided to terminate the ride, whichever came first. Subjects were asked to keep their heads as stable as possible during the ride. After ride termination, the MSAQ was completed.

For the Coriolis cross-coupling provocation of MS, subjects were seated on the motorized chair (Stille-Werner) with seatbelts fastened. A 5-min baseline recording of forehead skin conductance was performed while the subjects were seated with closed eyes. During the experiment, subjects were blindfolded and were asked to tilt their head as instructed by the operator. Commands for head tilts were given randomly in four directions, right, left, up, and down, at a frequency of 16 tilts/min (13). Rotation commenced with a constant acceleration of $1°/s^2$ until a maximum speed of 200/s was reached; subsequently, the speed was kept constant for the rest of the study. The rotation lasted for 15 min or until subjects felt uncomfortable and decided to terminate the ride; this time included chair acceleration/deceleration. After the termination of rotation, MSAQ was completed similar to the VR study.

Data analysis. Statistical analysis was performed using Prism 7 (GraphPad). Significance of the differences in nausea onset time, maximum nausea rating, and ride duration between the two conditions was assessed using paired *t*-tests. Significance of differences in MSAQ scores (total scores, individual symptom scores, and symptom categories) was assessed using two-way ANOVAs for repeated measures followed by corrected multiple-comparison tests; independent variables were stimulation type (VR and RC) and time (pre- and posttest). Significance of differences in SCL parameters (tonic level, frequency, and amplitude of transients) was assessed using two-way ANOVA for repeated measures followed by corrected multiple-comparison tests; independent variables were stimulation type (VR and RC) and nausea level. Šídák method was used to correct the multiple-comparison tests. Before correlational analysis was performed, relevant data sets were checked for normality using D'Agostino-Pearson and Shapiro-Wilk tests. We then used Spearman correlation test for the data sets with non-Gaussian distribution and Pearson correlation for normally distributed data. Data are presented as means ± standard error of the mean. Statistical significance was set at $P < 0.05$ with 95% confidence interval (CI).

RESULTS

Nausea onset time. There was no difference in nausea onset time between VR and RC stimulations (62 ± 10 and 51 ± 11 s, respectively; $P = 0.57$). There was a moderate but statistically significant correlation in the nausea onset time between the two studies ($r = 0.40$, $P = 0.034$; Fig. 1). Only one participant was able to conclude both VR and RC tests.

There was a weak but statistically significant negative correlation between the nausea onset time and the maximum nausea ratings in VR and RC studies ($r = -0.42$, $P = 0.02$ and $r = -0.37$, $P = 0.048$, respectively; Fig. 2, *A* and *B*). Removal of outliers resulted in a small reduction in the correlation coefficient in Fig. 2*A* (to $r = -0.35$, 0.048) and a loss of significance in Fig. 2*B*. Interestingly, there was also a moderate negative correlation between the nausea onset time in the VR study and the maximum nausea rating in the RC study and vice versa: in other words, those who developed nausea earlier had a higher maximum nausea rating not only in the same experiment, but also in the other study ($r = -0.46$, $P = 0.009$ and $r = -0.39$, $P = 0.03$, respectively; Fig. 2, *C* and *D*). Removal of obvious outliers seen in Fig. 2, *C* and *D*, resulted in a change in the correlation coefficient in Fig. 2*C* ($r = -0.39$, $P = 0.031$) and loss of significance in correlation in Fig. 2*D* ($r = -0.33$, $P = 0.071$).

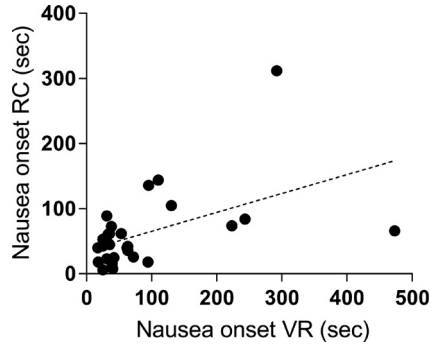

Fig. 1. Correlation between nausea onset times in rotating chair (RC) and virtual reality (VR) stimulations.

MSSQ scores, tolerance time, and nausea ratings during experiments. MSSQ scores varied greatly between participants; they ranged from 0 to 82.9 (mean = 26.6 ± 21.0). All participants reported some level of nausea during both experiments. The majority of the participants (29/30) could not complete both VR and RC tests. The mean tolerance time was significantly longer in the VR ride compared with the RC test (3.6 ± 0.4 vs. 6.0 ± 0.6 min, respectively; $P < 0.001$; Fig. 3*A*). There was no correlation between the tolerance times between the two conditions. The mean values for the maximum nausea rating (i.e., the ratings at which participants requested to terminate the experiment) were 6.5 ± 0.3 and 6.2 ± 0.2 for RC and VR conditions, respectively, with no significant difference between them. Maximum nausea rating in VR experiment was significantly correlated with the maximum nausea ratings in the RC test ($r = 0.58$, $P = 0.001$) as illustrated in Fig. 3*B*.

Symptom scores by MSAQ. When assessed immediately after the experiments, two-way ANOVA on the total symptom score showed no significant interaction between stimulation type and time [$F(1, 29) = 0.9758$, $P = 0.334$]. The multiple-comparison tests showed that the time factor did cause significant differences in both conditions. Subjects reported significantly higher MSAQ total symptom scores following both the RC stimulation and the VR ride compared with values reported before the experiment [mean difference (mean diff) = −1.71, CI = (−1.91, −1.5), $P < 0.0001$ and mean diff = −1.59, CI = (−1.79, −1.39), $P < 0.0001$, respectively; Fig. 4*A*]. Total MSAQ scores were not significantly different when two stimulation methods were compared in the same time points.

There was no significant interaction between stimulation type (RC vs. VR) and time (before vs. after) in scores of each

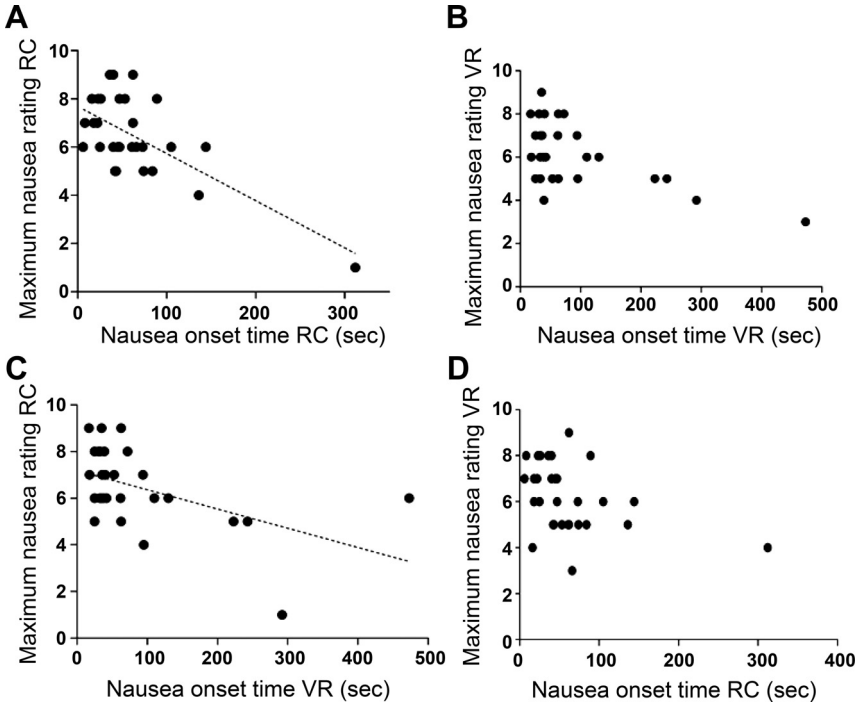

Fig. 2. Correlation of time of nausea onset in rotating chair (RC) experiment and maximum nausea rating in RC (*A*), correlation of time of nausea onset in virtual reality (VR) experiment and maximum nausea rating in VR (*B*), correlation of nausea onset time in VR and maximum nausea rating in RC (*C*), and correlation of nausea onset in RC study and maximum nausea rating in VR (*D*).

category of symptoms [*category 1*: $F(1, 29) = 2.938$, $P = 0.091$; *category 2*: $F(1, 29) = 3.759$, $P = 0.062$; *category 3*: $F(1, 29) = 0.001$, $P = 0.901$; and *category 4*: $F(1, 29) = 0.9784$; $P = 0.33$]. However, multiple-comparison tests revealed significant differences in category scores between two time points (before vs. after) in both stimulation methods (Table 1). There were no significant differences in scores of each category in a single time (before vs. after) when two stimulation types were compared.

The total postexperiment MSAQ scores obtained in both stimulations correlated substantially and highly significantly ($r = 0.69$, $P < 0.0001$; Fig. 5*A* and Table 2). Similarly, there was a significant correlation for each MSAQ category subscores between both stimulations (Fig. 5, *B–E*, and Table 2). There was no significant difference between the total score or any of the subscore mean values in both conditions.

Table 3 describes individual symptoms reported by the participants after both studies. There was a significant correlation between both studies in all symptoms except feeling sick in the stomach. The scores for 2/18 symptoms (lightheadedness and annoyed) were weakly correlated and nearly significant ($r = 0.31$, $P = 0.088$ and $r = 0.34$, $P = 0.058$, respectively). The two-way ANOVA interaction of stimulation type and nausea level (no nausea vs. maximum nausea) was not significant in 15/18 of symptoms. Multiple-comparison tests showed no significant differences in symptom intensity between the RC and VR stimulation methods. However, there was a significant interaction between stimulation type and nausea level in 3/18 symptoms (spinning, disorientation, and "sensation of vomiting"; $P < 0.001$, $P < 0.047$, and $P < 0.041$, respectively). Grouped decomposition of these three symptoms revealed that participants rated significantly higher in the RC study compared with the VR study (Table 3).

Relations between nausea level and skin conductance. An example of the forehead skin conductance recordings (with nausea ratings) obtained in one subject during the VR and RC

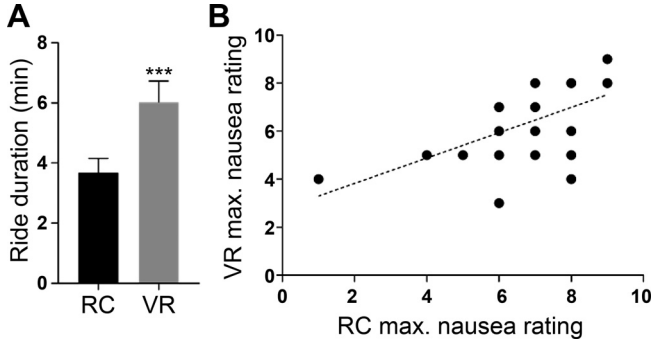

Fig. 3. Ride duration of virtual reality (VR) vs. rotating chair (RC; *A*) and maximum (max.) subjective nausea rating in 2 conditions (*B*). Note that the data are shown for 30 participants, and apparent smaller number of points on the graph is due to overlap in several instances as scores were integer values. ***$P < 0.001$.

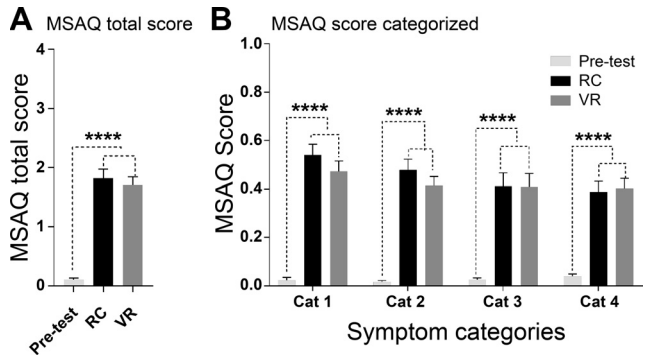

Fig. 4. Postexperiment symptoms evaluation. Total symptom score before and after virtual reality (VR) and rotating chair (RC) experiments (*A*) and subcategory (Cat 1–4) symptom scores (*B*) are shown. ****$P < 0.0001$. MSAQ, Motion Sickness Assessment Questionnaire.

Table 1. *Baseline vs. after-test-exposure MSAQ scores in each category of symptoms for RC and VR stimulation*

Category of Symptoms	Stimulation	Mean Difference, CI, *P* Value
Category 1: gastrointestinal	RC	−0.516, (−0.581, −0.451), <0.0001
	VR	−0.451, (−0.515, −0.385), <0.0001
Category 2: central	RC	−0.461, (−0.517, −0.406), <0.0001
	VR	−0.397, (−0.452, −0.342), <0.0001
Category 3: peripheral	RC	−0.386, (−0.459, −0.312), <0.0001
	VR	−0.384, (−0.458, −0.311), <0.0001
Category 4: sopite	RC	−0.349, (−0.413, −0.284), <0.0001
	VR	−0.387, (−0.451, −0.322), <0.0001

CI, confidence interval; MSAQ, Motion Sickness Assessment Questionnaire; RC, rotating chair; VR, virtual reality.

experiments conducted on different days is shown in Fig. 6. Four subjects were excluded from the skin conductance analysis due to excessive artifact in the recordings. There was no difference in the tonic forehead SCL signal at baseline on any of the stimulation types and no correlation between the two conditions (Fig. 6, *A* and *B*). Two-way ANOVA showed no significant interaction between stimulation type and nausea level in the tonic SCL [$F(1, 25) = 0.893$, $P = 0.35$]. However, the onset of nausea was associated with elevation in tonic SCL. In both VR and RC experiments, multiple-comparison test showed that the increasing trend of tonic SCL became significant at a time point associated with maximum nausea in comparison with the SCL during baseline [mean diff = 5.1, CI = (2.59, 6.97), $P = 0.007$ and mean diff = 1.49, CI = (0.47, 7.08), $P = 0.0001$, respectively; Fig. 7*A*]. There was no significant difference in tonic SCL between the stimulation types at time points associated with no nausea or maximum nausea. In fact, there was also a moderate correlation between the changes in the tonic skin conductance in both RC and VR stimulations ($r = 0.48$, $P = 0.04$; Fig. 7*C*).

There was minimal forehead phasic SC activity during baseline recording (Figs. 6 and 7*D*). Similar to tonic SCL, the interaction of stimulation type and nausea level was not significant [$F(1, 25) = 2.961$, $P = 0.097$]. The onset of MS symptoms was associated with an increase in the amplitude of the phasic skin conductance events; this elevation was substantial and significant at the time of the maximum nausea rating, causing an increase in the root-mean-square values of the spikes in both VR and RC experiments compared with baseline [mean diff = 0.27, CI = (0.091, 0.63), $P < 0.001$ and mean diff = 0.235, CI = (0.053, 0.851), $P < 0.006$, respectively; Fig. 7*D*]. There were no significant differences between the

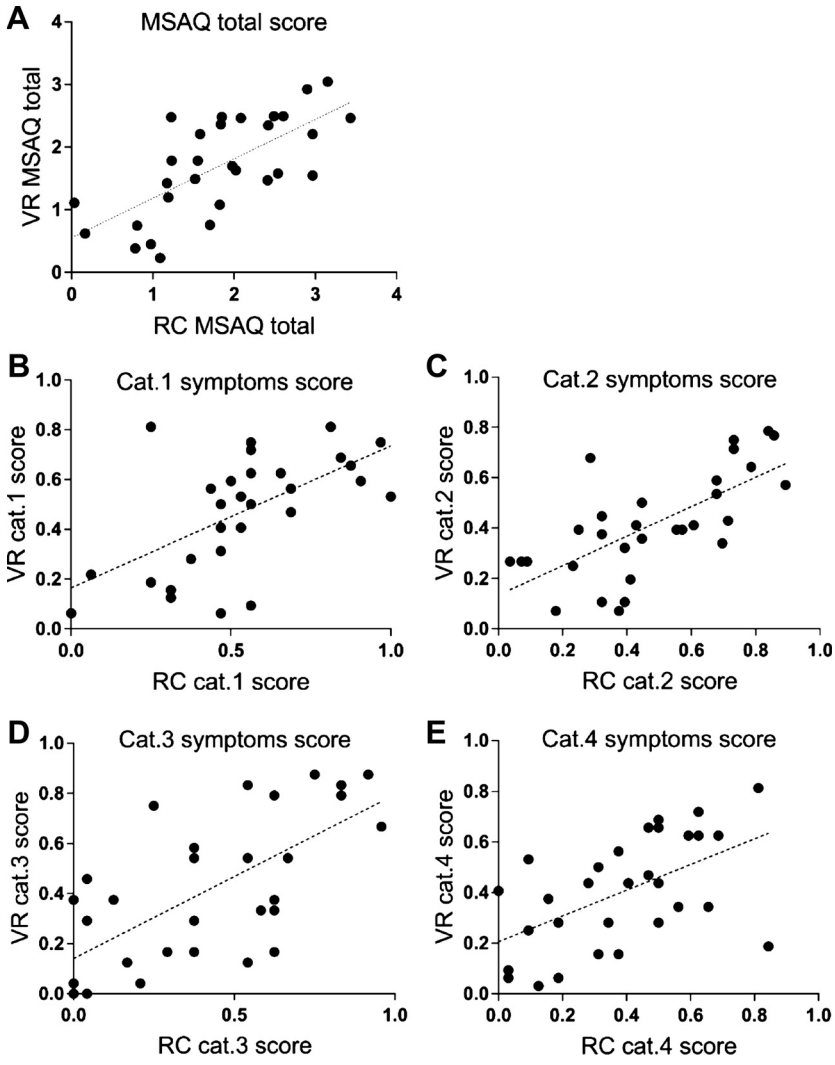

Fig. 5. Correlation of postexperiment symptoms in rotating chair (RC) vs. virtual reality (VR) conditions. *A*: total Motion Sickness Assessment Questionnaire (MSAQ) score. *B*: *category 1* (gastrointestinal). *C*: *category 2* (central). *D*: *category 3* (peripheral). *E*: *category 4* (sopitelike symptoms).

Table 2. *Mean postexposure scores, their comparison, and correlations for 4 motion sickness symptom clusters for VR and RC experiments*

	RC Study, Mean ± SE	VR Study, Mean ± SE	Mean Difference	Correlation
Total MSAQ	1.60 ± 0.04	1.81 ± 0.04	NS	$P < 0.0001$, $r = 0.69$
Gastrointestinal	0.53 ± 0.04	0.47 ± 0.04	NS	$P = 0.0005$, $r = 0.59$
Central	0.47 ± 0.04	0.41 ± 0.03	NS	$P < 0.0001$, $r = 0.69$
Peripheral	0.41 ± 0.04	0.40 ± 0.05	NS	$P < 0.0001$, $r = 0.67$
Sopite	0.38 ± 0.04	0.40 ± 0.04	NS	$P = 0.001$, $r = 0.54$

MSAQ, Motion Sickness Assessment Questionnaire; NS, not significant; RC, rotating chair; VR, virtual reality.

stimulation types in any time point associated with no nausea and maximum nausea. Although the frequency of the phasic SCL events tended to increase with increasing nausea ratings, this change did not become significant in either of the studies (Fig. 7*E*).

DISCUSSION

The aim of this study was to compare subjective symptoms and physiological effects of motion sickness induced by physical motion and by immersion in VR. For the former, we used a well-characterized-in-the-vestibular-research and highly provocative stimulus: rotation around vertical axis with head tilts known as Coriolis cross-coupling stimulation (4, 13). For the latter, we used a version of a virtual ride on a roller coaster that had proven provocative potential in our previous experiments (10, 27, 32). To the best of our knowledge, this is the first study where the same participants were subjected to two classes of provocative stimuli, allowing direct comparison of sensitivity to these stimuli as well as comparison of symptoms and major physiological effects accompanying the two types of motion sickness. There are three main findings in this study. First, sensitivity to both provocations (operationalized as latency to nausea onset) correlated between RC and VR studies. Second, both provocations resulted in the development of similar symptom profiles that closely correlated within individuals. Finally, we found that increases in forehead skin conductance paralleled progression of nausea in both condition.

Is there a relationship between sensitivity to vestibular and VR provocations? Sensitivity to different aversive stimuli could be assessed in a number of ways, the simplest of which being a comparison of the time to the onset of an unpleasant sensation and the duration of time during which one could tolerate it. In our case, these measures are represented by latency to nausea onset and by ride tolerance time. It must be acknowledged that the nature of our two stimuli was fundamentally different not only in their sensory modality, but also in their progression. Specifically, VR ride started right from a "fall" from a rather high point, and prominent virtual accelerations, linear as well as angular, were present throughout the ride. In other words, although provocative potential of VR content varied from moment to moment, overall there was no gradual progression of this potential, in contrast to RC condition where head tilts became more and more provocative with increasing angular velocity of the chair (see METHODS for the explanation of why this protocol was implemented). Because of this limitation, comparing absolute values of latency with nausea onset and of nausea tolerance time between the two conditions was not a valid approach. On the other hand, our correlational data for the latency to nausea onset indicate that those who were more sensitive to VR provocation were also more susceptible to vestibular stimuli. It must be acknowledged, however, that this correlation was weak to moderate. The weak-to-moderate correlation values can be attributed to

Table 3. *Mean MSAQ postexposure scores, their comparison, and correlations for individual motion sickness symptoms for VR and RC experiments*

Symptom Clusters	Individual Symptoms	Post-RC, Mean ± SE	Post-VR, Mean ± SE	Statistical Difference	Correlation
Category 1: gastrointestinal	Q1: Sick in the stomach	4.0 ± 0.4	3.3 ± 0.4	NS	None
	Q5: Queasy	4.1 ± 0.4	4.0 ± 0.3	NS	$r = 0.59$, $P = 0.0006$
	Q11: Nausea	4.8 ± 0.3	4.7 ± 0.4	NS	$r = 0.69$, $P < 0.0001$
	Q15: About to vomit	4.2 ± 0.4	3.0 ± 0.4	$P = 0.038$	$r = 0.31$, $P = 0.0892$
Category 2: central	Q2: Faintlike	2.8 ± 0.4	2.5 ± 0.3	NS	$r = 0.36$, $P = 0.0448$
	Q6: Lightheadedness	4.1 ± 0.3	3.6 ± 0.3	NS	$r = 0.31$, $P = 0.088$
	Q9: Disoriented	4.2 ± 0.5	3.3 ± 0.4	$P = 0.031$	$r = 0.52$, $P = 0.0029$
	Q13: Dizzy	5.0 ± 0.4	4.7 ± 0.3	NS	$r = 0.61$, $P = 0.0003$
	Q14: Spinning	5.2 ± 0.4	3.9 ± 0.4	$P = 0.003$	$r = 0.48$, $P = 0.0068$
Category 3: peripheral	Q4: Sweaty	3.6 ± 0.5	3.5 ± 0.4	NS	$r = 0.68$, $P < 0.0001$
	Q12: Hot	2.7 ± 0.4	3.2 ± 0.4	NS	$r = 0.60$, $P = 0.0004$
	Q8: Clammy/cold sweat	3.5 ± 0.5	3.1 ± 0.5	NS	$r = 0.63$, $P = 0.0002$
	Q18: Temperature discomfort	2.0 ± 0.4	1.5 ± 0.4	NS	$r = 0.51$, $P = 0.0039$
	Q17: Need for fresh air	3.4 ± 0.5	3.4 ± 0.5	NS	$r = 0.54$, $P = 0.0020$
Category 4: sopite	Q3: Annoyed	2.4 ± 0.4	2.5 ± 0.4	NS	$r = 0.34$, $P = 0.0587$
	Q7: Drowsy	3.0 ± 0.4	3.0 ± 0.4	NS	$r = 0.44$, $P = 0.0149$
	Q10: Tired	2.5 ± 0.4	3.0 ± 0.4	NS	$r = 0.46$, $P = 0.0096$
	Q16: Uneasy	4.4 ± 0.4	4.3 ± 0.4	NS	$r = 0.47$, $P = 0.0075$

MSAQ, Motion Sickness Assessment Questionnaire; NS, not significant; Q, quartile; RC, rotating chair; VR, virtual reality.

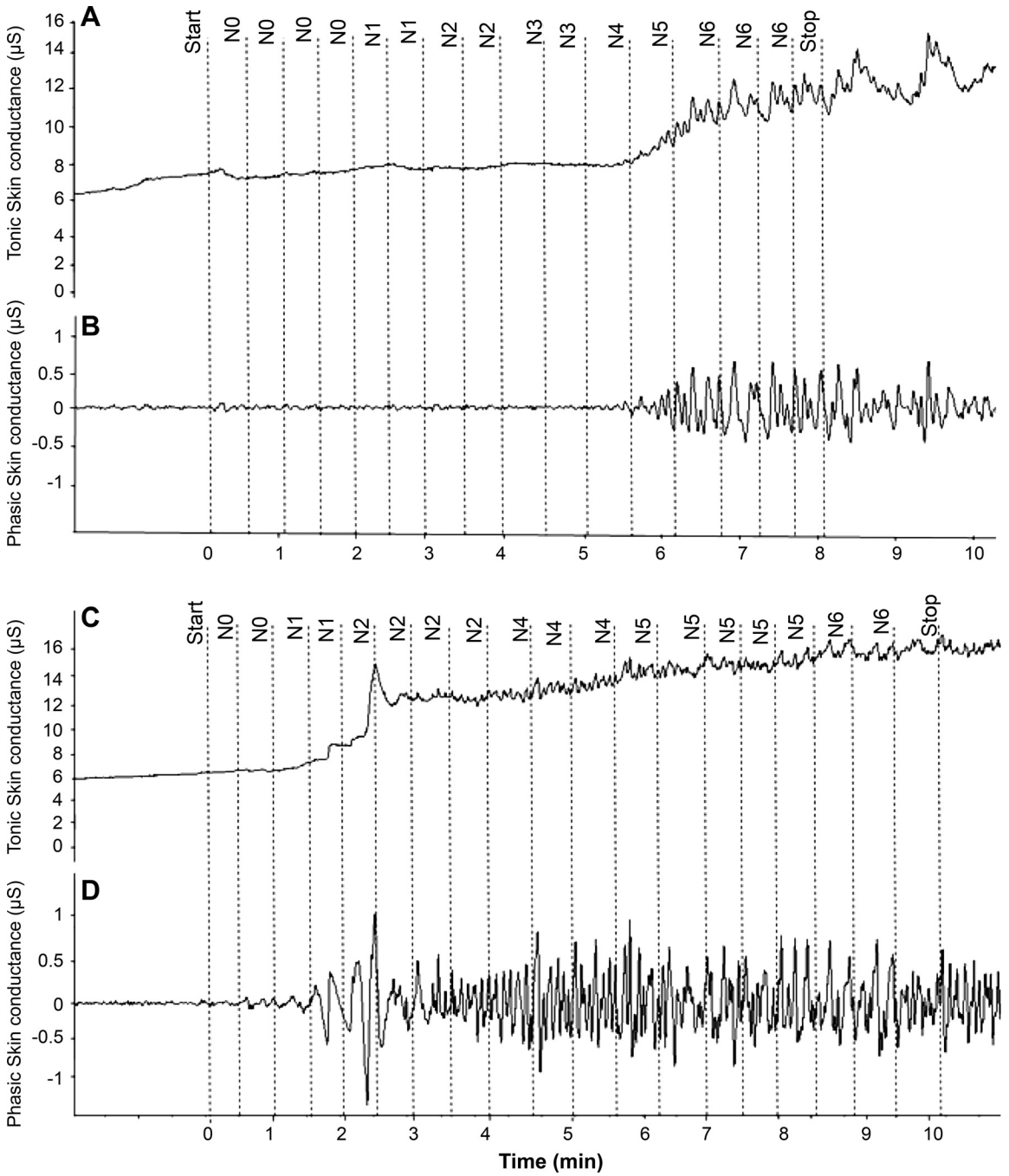

Fig. 6. An example of physiological recording during rotating chair (RC) and virtual reality (VR) experiments. Tonic skin conductance during RC stimulation (*A*), phasic skin conductance in RC stimulation (*B*), tonic skin conductance during VR stimulation (*C*), and phasic skin conductance during VR stimulation (*D*) are shown. N, subjective nausea level reported by participant on a 0- to 9-point scale.

the low power of the study caused by the limited number of participants in the study.

The maximum level of nausea induced by either provocation might serve as index of sensitivity to these stimuli only under the condition that they have similar duration; this was not the case in our study. The fact that maximum nausea levels correlated between VR and RC condition can be simply interpreted as an indication of similar subjective tolerance limits in both conditions for each subject. We did not find a correlation of ride tolerance time between the two conditions; this could mean either that there are no relationships between the two variables or that it was obscured by the differences in temporal dynamics between the two provocations (as outlined in the previous paragraph).

Interestingly, the latency to nausea onset negatively correlated with the maximum nausea reported by the subjects in both experiments. That is, subjects with shorter onset time reported higher nausea ratings at the end of the experiment and tolerated a shorter duration of exposure. One possible explanation of this finding is that subjects who reported an early

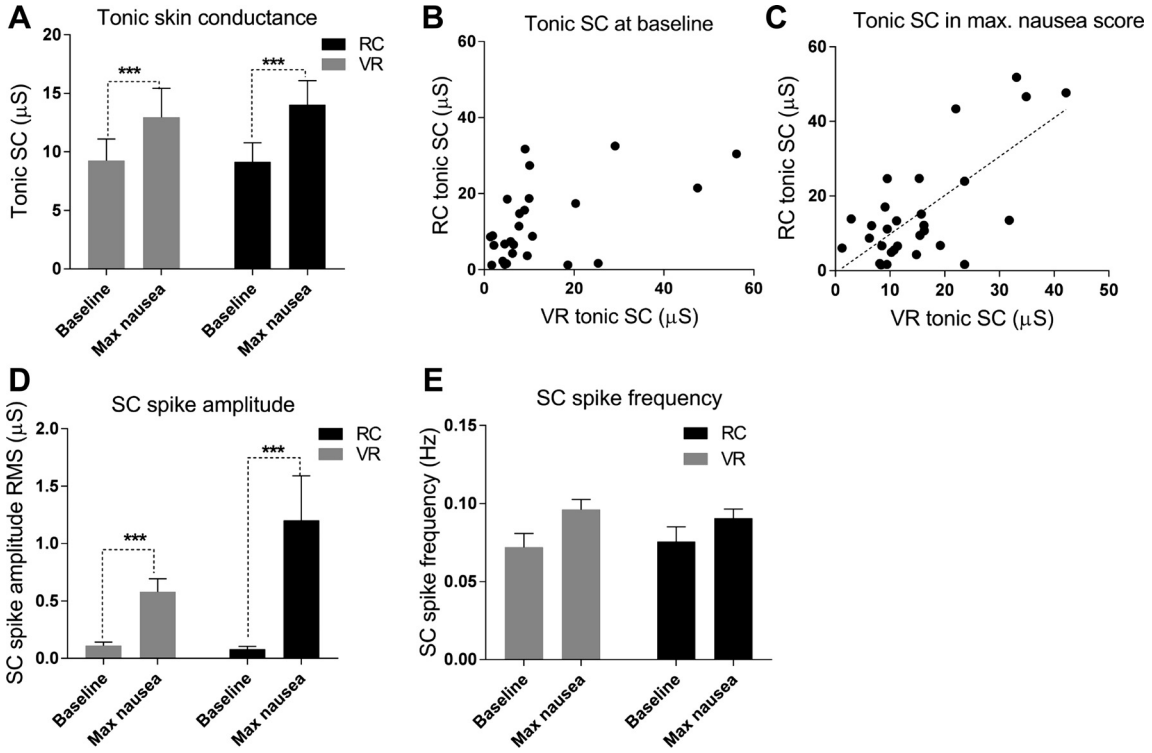

Fig. 7. Tonic and phasic skin conductance levels (SCL) in maximum (Max) nausea rating and baseline. Tonic SCL (*A*), correlation of tonic SCL at baseline (*B*), correlation of tonic SCL at time point with maximum subjective nausea rating (*C*), phasic spike amplitude root mean square (RMS; *D*), and phasic event frequency (*E*) are shown. ***$P < 0.001$. RC, rotating chair; VR, virtual reality.

onset of nausea continued to develop symptoms more rapidly as the experiment proceeded; on the other hand, individuals with a longer onset time developed symptoms slower and thus were able to tolerate longer exposure. Furthermore, we consider the finding of negative correlation between the nausea onset time in one study and maximum nausea rating in the other study of special interest, suggesting that subjects who experienced nausea in the early stages of a test reported higher nausea in both studies and vice versa. It must be acknowledged that after removal of outliers, these correlations became weak to moderate and in some cases were largely dependent on one or two subjects. Nevertheless, these correlations provide an indication that nausea onset time in one study could to some extent predict how a subject would feel in another study.

Is cybersickness a separate clinical entity? Clarifying the question of whether cybersickness is clinically different from classic, motion-induced motion sickness was one of our principal aims. For this purpose, we subjected the same cohort to visual and vestibular provocations and followed this by quantifying their symptoms using MSAQ, the most frequently used and well-validated tool for assessment and profiling motion sickness (11). Similar to our previous work where virtual ride was the only provocative stimulus (10, 27), we found that the dominating symptoms in VR condition were the gastrointestinal ones, followed by central, peripheral, and sopitelike symptoms (see METHODS). Likewise, symptoms reported by our participants during RC provocation are in good accord with previous studies investigating motion sickness induced by provocative motion (11, 20, 31).

While comparing and analyzing our MSAQ data, we targeted two specific questions: *1*) whether there were any differences in total MSAQ scores, in scores for the symptom clusters, or in the individual symptom scores between the two experimental conditions; and *2*) whether there was a within-subject correlation for all of these scores. Comparison of mean values for the total scores and for the cluster scores did not reveal any differences between the conditions, thus favoring the view that they represent essentially the same clinical entity. This was supported by substantial and highly significant correlations between the score pairs. Detailed comparison of individual symptom scores was generally in accord with findings for total and cluster scores: indeed, mean values did not differ for 15 out of 18 symptoms; of those, the highest correlation was found for feeling queasy or nauseous, dizzy, sweaty, and hot. Of the remaining 3 (about to vomit, feeling spinning, and disoriented), higher values were reported for RC stimulation. We propose that the difference in the sensation of about-to-vomit rating could be explained by the fact that the very termination of RC provocation (i.e., chair deceleration) was by itself an additional provocative factor. Indeed, whereas the action of VR provocation terminated immediately following subjects' request, chair deceleration must have induced an additional activation of vestibular receptors in semicircular canal, possibly resulting in stronger subjective sensation of near-vomiting. This same receptor activation triggered by a transition from a rotation at constant angular velocity to angular deceleration also provokes a sensation of spinning that likely resulted in higher rating for this symptom in RC condition.

One potential confounding factor that might have affected our conclusions could be different levels of severity of motion sickness between the two conditions. We argue here that in

both instances, our participants reached reasonably similar levels of aversion, that is, the state when they felt too uncomfortable to continue the experiment. This is supported by similar maximum nausea ratings reported during the two provocations and in the subsequent MSAQ ratings. Overall, our analysis suggests that the clinical picture of advanced motion sickness (assessed as a spectrum of symptoms and as their intensity) is very similar, independently of whether it is induced by pure visual or pure vestibular stimuli. This conclusion contradicts previously published results, and below we present our view on the potential causes of this controversy.

The principal sensory input responsible for provoking cybersickness is visual, and this places cybersickness close to simulator sickness that has been extensively studied (5, 21). Although simulator sickness shares many common symptoms with classic motion sickness, some substantial differences have been reported between them. One of the most influential papers on this subject (22) summarized several studies focused either on simulator sickness or on seasickness and concluded that symptom profile was substantially different. Although during seasickness, the dominant symptom was nausea followed by oculomotor and disorientation, simulator sickness has the consistent pattern of "oculomotor > nausea > disorientation." We propose that the cause of this difference may have been various degrees of severity of a condition: it is hard to imagine that if participants of simulator studies progress to near-vomiting, they still would rank nausea as less disturbing compared with oculomotor symptoms. We thus propose that the latter dominated at early stages of simulator sickness (especially when cathode-ray tube computer monitors were used), and because exposure to provocative stimulation terminated before the tolerance limit, participants had relatively low nausea ratings. Broadly speaking, symptom profiles may vary greatly with a progression of a disease (e.g., common cold starts from fatigue, but most disturbing symptoms at its peak are blocked nose and headache). As outlined in the previous paragraph, our participants terminated exposure at their individual tolerance limit, and we thus compared symptoms at as close a motion sickness severity as reasonably possible; we consider this to be a strong methodological aspect of our study. On the other hand, it remains plausible that symptom profile may differ and depend on provocation type during earlier, nonadvanced stages of MS; one way of clarifying this issue in the future could be by using a shortened form of the MSAQ.

Another methodological strength of this study is that the same cohort of volunteers was subjected to the two types of provocative stimuli. The importance of this factor is best illustrated by a work that compared symptom profiles and severity of MS induced by flight simulators to those induced by immersion in VR (41). Apart from differences in the profiles, comparison revealed that total symptom scores during cybersickness were about three times higher compared with simulator sickness. One factor that potentially accounted for this difference (and acknowledged by the authors) was different study populations: mostly male military aviators who were self-selected to be resistant to motion sickness in simulator studies and nonpreselected college students, with 50% women, in cybersickness studies. Our experimental design completely eliminated this factor and allowed the most accurate comparison of symptoms obtained in both conditions in the same individuals. Of note, despite relatively small sample size, our participants represented a very broad spectrum of MS susceptibility as was documented by their MSSQ scores.

We have limited our physiological measurements to forehead skin conductance. Among all reported autonomic and biochemical variables (with the exception of plasma vasopressin; Ref. 24), forehead sweating rate is by far the most sensitive and one of the most specific changes during motion sickness. Indeed, we (10, 27) and others have demonstrated only minor or moderate effects of motion sickness on heart and respiratory rate, arterial pressure, heart rate variability, body temperature, or gastric myoelectric activity (16, 30, 52). In contrast, rise in sweating rate is quite dramatic as shown in the current study and as was demonstrated previously for both visually induced MS (10, 27, 50) and during motion provocation (13, 14, 51). Furthermore, forehead sweating correlates with subjective nausea rating (Refs. 10, 13, 27 and current study), whereas changes in other autonomic measures (finger skin conductance, heart and respiratory rate) could be associated with arousal provoked by the onset of real or virtual motion (10, 28), making it difficult to identify and measure the response component related to motion sickness. Overall, our results are in good accord with the previous studies of MS evoked by different provocations, where sweating responses were prominent (13, 14). In all participants, there was either minimal or no SCL activity on the forehead during baseline; in contrast, there was a significant increase in SCL when nausea level was high. Consistently with similarity in subjective symptoms, we did not find any differences in forehead sudomotor responses between the two provocations.

We have previously addressed the question of why motion sickness is associated with "thermoregulatory" forehead sweating (33) by expanding Treisman's (47) hypothesis of the "toxic" origin of nausea during MS. Treisman has proposed that the brain erroneously interprets a visual-vestibular sensory mismatch as a sign of intoxication, and nausea provides a mechanism of aversive conditioning to prevent future toxin ingestion. If this is correct, it would be reasonable to suggest that other protective responses might be triggered by the same stimuli. It has been shown in rodents that reducing body temperature during intoxication is an adaptive survival strategy (40), and we suggest that this could represent a key to understanding thermoregulatory disturbances during MS. Indeed, looking at MS from this perspective, it becomes apparent that it is in fact associated with a complex integrative response including physiological (sweating, cutaneous vasodilation; see Ref. 33 for review), behavioral (cold-seeking; Ref. 37), and cognitive (altered perception of ambient temperature; Ref. 37) components that eventually leads to a fall of body temperature in humans (36). Confirming this hypothesis, we have recently discovered that provocative motion also elicits profound hypothermic responses in rats, musk shrews (7, 35), and mice (49); this hypothermia was preceded by prominent cutaneous vasodilation, a major heat-loss mechanism in rodents that is homologous to sweating in humans.

Conclusions and perspectives. We compared the sensitivity to and the effects of the two different motion sickness-inducing provocations; we conducted both studies in the same cohort and collected subjective ratings when participants were in a reasonably comparable severity state of sickness. Despite fundamental differences in provoking stimuli and, consequently, in sensory inputs responsible for development of motion sick-

ness, it appears that symptoms and autonomic changes were similar during VR and vestibular stimulation. We thus conclude that cybersickness and classic motion sickness are clinically identical, at least in their advanced stages. Since the temporal progress of the symptoms was not investigated in this study, it remains possible that symptom spectrum differs during onset and early development of these malaises.

Sensitivity to vestibular provocations could be reduced by repetitive exposure to provocative motion; this forms the basis for motion sickness desensitization, a recognized intervention in Air Force pilot training programs (1, 4, 9). These programs are, however, time consuming (weeks) and require expensive equipment items. It is currently unknown whether desensitization occurs in the vestibular sensors in the inner ear, in central vestibular pathways, or at higher levels where visual and vestibular stimuli interact. There is limited evidence in favor of the latter: two studies reported cross-desensitization, when repetitive exposure to optokinetic drum reduced susceptibility to seasickness (39, 48). Our finding of moderate correlation in sensitivity to visual and vestibular stimuli indirectly supports the possibility of cross-desensitization, as it is reasonable to suggest that reducing sensitivity to one type of provocation can result in reduction in susceptibility to another type. Another potential practical implication of our results is using VR technology for identification of MS-susceptible individuals, an essential task for occupational health and safety in professions where MS represents a risk of safety hazard.

GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

F.R.W., D.M.H., and E.N. conceived and designed research; A.M.G. and E.N. performed experiments; A.M.G. and F.R.W. analyzed data; A.M.G., F.R.W., D.M.H., and E.N. interpreted results of experiments; A.M.G. prepared figures; A.M.G. drafted manuscript; F.R.W., D.M.H., and E.N. edited and revised manuscript; A.M.G., F.R.W., D.M.H., and E.N. approved final version of manuscript.

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