# Assessment of Olfactory Perception in Individuals with Motion Sickness

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**BACKGROUND:** Individuals who experience motion sickness (MS) frequently mention the presence of smells in the environment as a factor favoring the occurrence of MS symptoms. The aim of the present work was to compare olfactory function in MS sensitive (MS+) and insensitive (MS-) subjects.

- **METHODS:** Olfactory testing included determination of odor detection thresholds, subjective evaluation of the quality (intensity, hedonicity, and familiarity) of three different odorants (limonene, isovaleric acid, and petrol) as well as measures of skin conductance responses to these three odorants.
- **RESULTS:** Results showed no difference in olfactory sensitivity between MS+ and MS- subjects. However, findings of both subjective (odor quality self-rating) and objective (psychophysiological responses) measures did reveal that the affective response to petrol odor was significantly different in MS+ and in MS- subjects. Indeed, on a scale from 0 (unpleasant) to 10 (pleasant) MS+ subjects rated petrol odor as more unpleasant (mean = 2.52) than MS- subjects (mean = 4.15) and rise-time of skin conductance responses to petrol odor was significantly longer in MS+ (mean = 5.98 s) compared to MS- subjects (mean = 3.22 s).
- **DISCUSSION:** Our study delves further into the knowledge of the relationship between motion sickness and olfaction by demonstrating a modified olfactory perception in motion sickness sensitive subjects at both the psychophysical and psychophysiological levels.
- KEYWORDS: motion sickness, olfactory detection thresholds, odor subjective ratings, skin conductance response.

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**T**ravel in modern vehicles (cars, boats, planes, helicopters, spacelab, etc.) can cause a large panel of symptoms such as nausea, headache, and postural discomfort, which are defined as motion sickness (see Golding<sup>14</sup> for review). Anyone with a healthy vestibular system can become motion sick with a sufficiently provocative and long motion stimulus. For this reason, a variety of research has been conducted to get a better understanding of this problem. In addition to being unpleasant, it has been highlighted that motion sickness can negatively affect performance of complex tasks requiring sustained performance.<sup>20</sup> In particular, motion sickness can even slow field and simulator training for pilots and aircrew.<sup>5</sup>

Three main theories offer a clear explanation about motion sickness mechanisms. The 'toxin detector' hypothesis<sup>33</sup> suggests that the brain can identify any mismatch of expected patterns of vestibular, visual, and kinaesthetic cues as a sign of central nervous system breakdown and a possible ingested neurotoxin, and thus will initiate vomiting as a defense mechanism. The

vestibular–cardiovascular reflex hypothesis<sup>4</sup> defines motion sickness as a consequence of visceral discomfort after activation of vestibular autonomic reflexes due to the convergence of vestibular and autonomic afferent information in the brainstem and cerebellum. The most widely accepted theory is the sensory conflict or sensory mismatch theory,<sup>29</sup> which postulates that motion sickness originates from a sensory mismatch between actual vs. expected invariant patterns of vestibular, visual, and somatosensory inputs. However, whereas motion sickness mechanisms are now well understood by the scientific

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community, there is still no actual behavioral or pharmaceutical technique that could cure motion sickness without side effects.

Motion sickness could be influenced by several factors, such as no view of the road ahead,<sup>34</sup> caloric food,<sup>10,22</sup> or nicotine.<sup>16</sup> Interestingly, the presence of strong smells in the environment has also been reported as a factor that may make motion sickness more likely to occur. More precisely, some authors suggested that unpleasant odors could contribute to motion sickness.<sup>10,13,34</sup> A recent study investigating motion sickness in rally car codrivers showed that onboard smells were one of the three main risk factors for motion sickness.<sup>27</sup> Recently, our team<sup>25</sup> evaluated more precisely the relationship between motion sickness and olfaction. In this study, subjects were exposed to three sessions of nauseogenic stimulation, offvertical axis rotation (OVAR), performed under conditions of olfactory stimulation with limonene (pleasant odor), petrol (unpleasant odor), or distilled water (as a control). Motion sickness was assessed before, during, and after each OVAR session. This study showed that OVAR consistently increased the induced motion sickness. However, the addition of an odor, whether pleasant or unpleasant, during the rotation did not affect the occurrence of motion sickness symptoms compared to the control condition. This study also showed that intensity of odors was significantly increased after OVAR and the intensity was significantly higher for an unpleasant odor than for a pleasant one. For the hedonicity, OVAR made the unpleasant odor more unpleasant, whereas the limonene odor was slightly more pleasant. Paillard et al.<sup>25</sup> highlighted the lack of influence of odors in motion-induced sickness, but demonstrated it as an impact of a nauseogenic test on olfactory perception. Following Paillard et al.,<sup>25</sup> one could question whether sensitivity to odors is higher in motion sickness sensitive subjects.

The aim of the present study was to compare olfactory function in motion sickness sensitive subjects and in motion sickness insensitive subjects using both psychophysical and psychophysiological measurement. Psychophysical measures included olfactory detection thresholds tests and self-rating of intensity, familiarity, and hedonicity of three odorants. In addition, psychophysiological responses to these odorants were analyzed using skin conductance measurements. Indeed, in the olfactory modality, it is well known that skin conductance can be modulated by the perception of an odorant<sup>30,35</sup> and specifically that it could be modulated by odor pleasantness.<sup>1,2</sup> Thus, it appears relevant to determine whether psychophysiological responses to odorants differ between motion sickness sensitive and insensitive subjects.

## **METHODS**

#### **Subjects**

The inclusion criteria of the present study were: 1) to be nonsmokers; 2) to report normal smell sensitivity and no history of nasal/sinus disease or extensive exposure to chemicals with potential toxicity; and 3) to be free of any vestibular and neurological disorders. A group of 85 healthy volunteers (students from the University of Franche-Comté) who fit with these inclusion criteria were asked to complete the Motion Sickness Susceptibility Questionnaire (MSSQ<sup>12</sup>). The first stage of the study was a triage phase where we made sure that our initially selected subjects had either a motion sickness – score B (MSB; during adulthood) equal or higher than 15 (thus belonging to the MS+ group) or below 2 (thus belonging to the MS- group). This criterion was decided according to Golding.<sup>15</sup>

Of these 85 students, 42 volunteers were asked and agreed to take part in the second stage of the study, i.e., olfactory testing. The sample of subjects included 34 women and 8 men; their ages ranged from 20 to 30 yr (mean age 22 yr, 4 mo).

The MS+ group, i.e., subjects who are very sensitive to motion sickness, included 21 subjects (19 women and 2 men, mean age 22 yr, 5 mo; MSB score range between 15 and 40.5). The MS- group, i.e., subjects who are not sensitive to motion sickness, included 21 subjects (15 women and 6 men; mean age 22 yr, 3 mo; MSB score range between 0 and 2).

The study was reviewed and approved by the local ethics committee and declared to the national authority (UF: 1013; DGS 2006/0494) in accordance with the Declaration of Helsinki on biomedical research involving human subjects. Participation required the completion of an informed consent form.

For electrodermal recordings 10 subjects in the MS+ group and 12 subjects in the MS- group were excluded due to low skin conductance responses (SCR < 0.02  $\mu$ S) as described below, or due to the lack of distinct SCRs during the entire experiment. Thus, 11 subjects in the MS+ group and 9 subjects in the MS- group were available for skin conductance data analyses.

#### Materials

Olfactory detection thresholds were determined using n-butanol  $(C_4H_{10}O;$  molecular weight = 74,12; Sigma-Aldrich, Saint Quentin Fallavier, France). A dilution series (factor 2) was prepared in odorless mineral oil (Sigma-Aldrich). After successive dilutions, the full series included steps 1 to 25 (step 25 is the highest concentration). Placed into glass tubes were 4 ml of each concentration (7.5 cm high, 1 cm in diameter at the opening). Another tube was filled with 4 ml of mineral oil only.

For subjective ratings and recording of skin conductance responses, three specific odorants were used: (R)-(+)-limonene ( $C_{10}H_{16}$ ; molecular weight = 136.23; Sigma-Aldrich), a pleasant orange-like odor; isovaleric acid ( $C_5H_{12}O_2$ ; molecular weight = 102.3; Sigma-Aldrich), an unpleasant cheesy odor; and petrol as a travel-related smell. The dilutions used in our study were determined according to a pretest carried out on 10 subjects. The dilutions that reached a moderate intensity perception were chosen for the tests. Specifically, limonene was used without dilution (100% of the stock solution), while isovaleric acid and petrol were diluted at 50% in mineral oil and at 25% in water, respectively. Nasal stimuli were presented in glass bottles (6 cm high, 2.5 cm in diameter at the opening) filled with 10 ml of each solution.

## Procedure

The experiment was carried out in two separate sessions. The first session was dedicated to the psychophysiological evaluation of olfactory function. Olfactory detection thresholds to n-butanol were determined using a classical ascending binary (stimulus vs. blank) forced-choice method. A trial consisted in the presentation of two tubes, one being the blank (mineral oil) and the other containing the dilution of the odorant (n-butanol). The subject indicated which one of the two randomly presented tubes contained the odorant. Even if no sensations were perceived or if no difference was apparent between the tubes, the subject was required to choose one tube or the other. No feedback was given regarding the correctness of the responses. Testing began at the weakest concentration so as to avoid olfactory receptor saturation. For each concentration, the test was performed three times. The olfactory detection threshold was determined when the subjects responded correctly three times at two consecutive concentration levels (for statistical analyses, the concentration step used was the first of both consecutive concentrations). Then, subjects were asked to rate the perceived intensity, hedonicity, and familiarity of limonene, isovaleric acid, and petrol using a Likert scale from 0 (weak, unpleasant, unfamiliar) to 10 (strong, pleasant, familiar). The order of odorants tested was counter-balanced across subjects. The interstimulus interval used between each odorant was 1 min ( $\pm$  10 s).

The second session was dedicated to the recording of skin conductance responses (SCR) to limonene, isovaleric acid, and petrol, which were presented in a random order. The SCRs, expressed in microSiemens (µS), were acquired using a BioPac MP150 system accompanying AcqKnowledge software (BioPac Systems, Goleta, CA). SCR was recorded through two Ag-Cl electrodes placed on the second and third fingers of a subject's right hand. The subjects were seated in a comfortable armchair in a quiet room (room temperature ranged from 20 to 22°C). When the electrodes were in position, the subject was told not to move and asked to relax to establish good baseline conductivity. Visual cues were excluded by a blindfold and auditory cues were excluded by a soundproof helmet. The session began with a rest period of 5-min duration. The nasal stimuli were presented at the outset of inspiration. According to the usual recommendations,<sup>11</sup> SCR data were as follows: phasic stimulus-elicited SCR amplitudes referring to the first response were equal to or greater than 0.02 µS with a minimal slope of 0.01  $\mu$ S  $\cdot$  s<sup>-1</sup>, which occurred with an interval of 0.5–6 s after the onset of the stimulus. For each of the observed SCR following the stimulation, the compound response was scored from the inflection point to peak. If more than one response occurred in the interval (0.5-6 s), only the first one was scored. The parameters used for statistical analyses were amplitude and rise-time. Testing was performed by experimenters blinded to the motion sickness status of the subjects.

#### **Statistical Analysis**

Data were statistically evaluated with Statistica 7.1 software using Student's *t*-tests for independent samples. Spearman rank tests were conducted on the whole sample (i.e., MS+ and

MS- groups) to study correlations between MSB scores and psychophysical (i.e., olfactory thresholds; odor intensity, familiarity, and hedonicity) and psychophysiological parameters (i.e., SCR amplitude and rise-time). Data were expressed as mean  $\pm$  SEM. The significant level was set as 0.05. The nonsignificant results were noted as n.s.

### RESULTS

The mean thresholds were based on the dilution steps (i.e., the concentration step at which subjects responded correctly three times). The statistical analysis showed no significant difference [t(40) = -1.82; P = 0.08] in olfactory sensitivity to n-butanol between the MS+ (mean thresholds =  $7.33 \pm 1.4$ ) and MS-groups (mean thresholds =  $10.9 \pm 1.3$ ).

The mean scores of perceived intensity, hedonicity, and familiarity of the three odorants tested (limonene, isovaleric acid, petrol) are presented in **Table I**. Our results showed that MS+ subjects rated the petrol odor as more unpleasant than MS- subjects [t(40) = -2.69; P = 0.01]. In addition, the perceived intensity of isovaleric acid was significantly higher in MS+ subjects than in MS- subjects [t(40) = 2.25; P = 0.03]. Concerning odor familiarity ratings, results showed a nonsignificant difference between MS+ and MS- subjects.

Mean values of the amplitude and rise-time of SCR to limonene, isovaleric acid, and petrol are given in **Table II**. For limonene and isovaleric acid our analysis did not show any significant difference between MS+ and MS- subjects either for SCR amplitude or for SCR rise-time. For petrol, there was no difference of SCR amplitude between MS+ and MS- subjects, but SCR rise-time was significantly higher in MS+ subjects compared to MS- subjects [t(18) = 2.85; P = 0.009].

The Spearman rank test conducted in the entire sample between MSB scores and psychophysical data showed no significant results except a negative correlation between MSB scores and isovaleric acid familiarity ratings (**Table III**). There

**Table I.** Mean Scores (and Standard Error of the Mean, SEM) of Perceived Intensity, Hedonicity, and Familiarity Obtained on the Psychophysical Scale for Limonene, Isovaleric Acid, and Petrol in MS+ and MS- Subjects, and Respective *t*-Values and *P*-Values.

	MS+	MS-	t(40)	P-VALUE
Limonene				
Intensity	5.43 (0.49)	6.27 (0.45)	-1.26	0.22
Hedonicity	5.69 (0.37)	5.93 (0.65)	-0.33	0.75
Familiarity	4.77 (0.59)	4.53 (0.46)	0.31	0.76
Isovaleric Acid				
Intensity	9.03 (0.18)	8.16 (0.36)	2.25	0.03*
Hedonicity	0.89 (0.19)	1.34 (0.34)	-1.17	0.25
Familiarity	1.13 (0.34)	2.27 (0.47)	-2.01	0.05
Petrol				
Intensity	8.02 (0.34)	8.03 (0.34)	-0.02	0.99
Hedonicity	2.52 (0.37)	4.15 (0.48)	-2.69	0.01*
Familiarity	7.86 (0.43)	7.10 (0.62)	1.03	0.31

The scales ranged from 0 (weak, unpleasant, unfamiliar) to 10 (strong, pleasant, familiar). Significant differences at least at P < 0.05 are marked with an asterisk.

**Table II.** Mean Values (and Standard Error of the Mean, SEM) of the A) Amplitude and B) Rise-Time of the Skin Conductance Responses to Limonene, Isovaleric Acid, and Petrol in MS+ and MS- Subjects, and Respective *t*-Values and *P*-Values.

	A. AMPLITUDE (μs)						
	MS+	MS-	<i>t</i> (18)	P-VALUE			
Limonene	0.71 (0.24)	1.76 (0.92)	-1.20	0.25			
Isovaleric acid	0.96 (0.31)	1.85 (0.78)	-1.12	0.28			
Petrol	0.99 (0.36)	1.19 (0.39)	-0.37	0.71			
	B. RISE-TIME (s)						
		B. RISE-TI	ME (s)				
	MS+	B. RISE-TI MS-	ME (s) t(18)	<i>P</i> -VALUE			
Limonene	<b>MS+</b> 5.24 (0.95)	<b>B. RISE-TI</b> <b>MS</b> - 3.76 (0.40)	ME (s) t(18) 1.33	<b><i>P</i>-VALUE</b> 0.20			
Limonene Isovaleric acid	<b>MS+</b> 5.24 (0.95) 5.78 (0.84)	<b>B. RISE-TI</b> <b>MS</b> – 3.76 (0.40) 3.89 (0.49)	ME (s) t(18) 1.33 1.83	<b><i>P</i>-VALUE</b> 0.20 0.08			

Significant differences at least at P < 0.05 are marked with an asterisk.

was also no significant correlation between MSB scores and psychophysiological data (Table III).

## DISCUSSION

The aim of the present study was to assess the relationship between olfaction and motion sickness susceptibility by comparing the olfactory function in subjects highly or not motion sickness sensitive. Firstly, our results showed similar olfactory sensitivity to n-butanol according to motion sickness susceptibility. Contrary to these findings, our pilot data<sup>24</sup> showed a decreased olfactory sensitivity in subjects with high motion sickness susceptibility compared to the not-motion sick subjects. The only difference between these two studies is the subjects' selection. Indeed, among 20 subjects, some smokers were selected in the pilot study, whereas no smokers were recruited in the present study. To date, it is well known that smoking can have an influence on olfactory perception, particularly on olfactory threshold (see Greenberg<sup>17</sup> for review) as well as on motion sickness susceptibility.<sup>16</sup> This first result underlined the importance of selecting only nonsmoking subjects to study the relationship between olfaction and motion sickness. This result also suggested that the olfactory function at peripheral level (odor acuity) is unaffected by motion sickness. Moreover, our study showed no difference of odor familiarity ratings between highly motion sick and not motion sick subjects, but did show interesting results for hedonicity and intensity according to motion sickness susceptibility. In this study, highly motion sick subjects rated petrol odor as more unpleasant than not-motion sick subjects. Our pilot data<sup>24</sup> showed that motion sickness sensitive subjects judged the odor of leather and petrol as more unpleasant than subjects who were not sensitive to motion sickness. Herz et al.<sup>18,19</sup> highlighted that olfactory hedonic responses could be modified in accordance with the emotional valence of the associated experience, i.e., the emotional context in which an odor is smelt could influence the perceived odor hedonicity in a constant way. It means that if a subject smells an odor in an unpleasant context, the subject will judge this odor as unpleasant afterward. According to this finding, we could suggest that subjects who are very sensitive to motion sickness perceive the odor of petrol as more unpleasant as it reminds them of the bad experience of motion sickness in vehicles. This idea leads to the hypothesis that olfaction can be conditioned by motion sickness. Arwas et al.<sup>3</sup> confirmed this hypothesis with taste aversion. The authors required their subjects to drink a flavored beverage and half of their subjects carried out a rotation-induced motion sickness. This study showed that the subjects receiving rotations consumed less drinks than the subjects who did not experience rotations. Klosterhalfen et al.<sup>21</sup> confirmed this finding using a Pavlovian conditioning. Using a novel taste (elderberry juice) as a conditioned stimulus and a vection motion as a nauseogenic test, the authors highlighted a taste aversion for the novel taste. We suggest that

**Table III.** Spearman's Correlation Coefficients and *P*-Values Between A) MSB Scores and Olfactory Thresholds; B) Subjective Rating of Odor Intensity, Familiarity, and Hedonicity; and C) SCR Amplitude and Rise-Time for the Whole Sample (i.e., MS+ and MS- Groups).

			MSB SCORES AND OLFACTORY THRESHOLDS			
Α.			r			Р
			-0.25			0.12
	MSB SCO	MSB SCORES AND INTENSITY FAMILIARITY			MSB SCORES AND HEDONICITY	
В.	r	Р	r	Р	r	Р
Limonene	-0.19	0.24	0.06	0.70	-0.12	0.48
Isovaleric Acid	0.30	0.06	-0.33	0.04*	-0.19	0.24
Petrol	0.03	0.83	0.13	0.43	-0.30	0.06
		MSB SCORES AND SCR AMPLITUDE			MSB SCORES AND SCR RISE-TIME	
с.		r	Р		r	Р
Limonene		0.01	0.96		0.10	0.67
Isovaleric Acid	_	0.10	0.68		0.25	0.28
Petrol	_	0.06	0.80		0.41	0.08

Significant differences at least at P < 0.05 are marked with an asterisk.

ness would lead to a similar olfactory aversion, which would explain our findings for petrol hedonicity. However, Paillard et al.<sup>25</sup> showed that petrol odor did not induce motion sickness more rapidly, but showed an influence of motion-induced sickness on this odor characteristic. In fact, these authors showed that the OVAR test seems to accentuate the perceived quality of odors: after the nauseogenic test smells are perceived as more intense, unpleasant odors are perceived as more unpleasant, and pleasant odors are perceived as more pleasant. This last result underlined that the negative experience of motion sickness tends to

pairing odors with motion sick-

increase the perceived quality of odors but seems to contradict the influence of emotional valence of the associated experience as explained above. Moreover, these findings also underlined that the negative experience of motion sickness influences the olfactory hedonicity but the hedonicity does not influence the induced-motion sickness.

Furthermore, the perceived intensity of isovaleric acid was significantly higher in highly motion sick subjects compared to not-motion sick subjects. As regards our previous findings, this is not explained by a difference in olfactory sensitivity between the two groups. Doty et al.<sup>9</sup> underlined a relationship between olfactory intensity and pleasantness. In fact, these authors showed that intensity and hedonicity are inversely related. However, hedonicity cannot explain the higher perceived intensity of isovaleric acid as the present study showed that highly motion sick subjects did not consider isovaleric acid as more unpleasant than not-motion sick subjects. In addition, results of the correlation analysis showed only a negative correlation between MSB scores and familiarity ratings of isovaleric acid, which was perceived as the most unpleasant odor (in either group). Again, this result cannot be explained by a difference in odor hedonic perception between MS+ and MSgroups. Similarly to Paillard et al.,<sup>25</sup> our results showed that motion sickness seems to modify the perceived quality of isovaleric acid, but further study would be necessary to better understand the influence of motion sickness on this odor.

Additionally, our results showed that for the odor of petrol, which was perceived as more unpleasant, SCR rise-time was significantly longer in highly motion sick subjects compared to not-motion sick subjects. Our measures of electro-dermal activity confirmed that skin conductance can be modulated by a smell perception<sup>30,35</sup> and specifically that it could be modulated by odor pleasantness.<sup>1,2</sup> However, the smell of petrol influenced the SCR rise-time but not the amplitude, which was against prediction. One possible explanation could be that the observed electrodermal activity modifications are sensitive to the hedonic valence of the odor for the subjects, although there is no change in their arousal. For some authors, the amplitude of the electrodermal responses are correlated with the arousal modifications regardless of emotional valence.<sup>6,32</sup> Additionally, the correlation analysis between MSB scores and psychophysiological parameters showed no significant results.

The skin conductance responses property is well-known as being closely associated with emotion and attention.<sup>12,23,28</sup> Regarding emotion, the previous paragraph underlined the lack of influence of emotional valence on olfactory perception associated with motion sickness. Interestingly, some studies underlined a common neuroanatomical pathway for odor hedonicity and attention. On one hand, Royet et al.<sup>31</sup> showed that the orbitofrontal cortex (OFC) activity was significantly higher during hedonicity judgments of different smells. On the other hand, Diekhof et al.<sup>8</sup> highlighted the role of the OFC in the prioritization of attentional selection. Our results would emphasize the relationship between attention and odor hedonicity but further studies would be necessary to confirm this hypothesis.

Finally, our study presents some limitations. Firstly, most of subjects were women. This is explained by the large number of women who are highly motion sick. However, as women demonstrate better olfactory abilities than men,<sup>7</sup> further studies with more men would be interesting. In addition, the age of the subjects ranged from 20 to 30 yr old while their susceptibility to motion sickness was related to adulthood. It is known that motion sickness is inversely related to the age. Paillard et al.<sup>26</sup> showed motion sickness decreases through the lifespan, testing healthy participants from 20 to 92 yr of age. The subjects' age range has been chosen to be quite small, and thus limits the age impact (as shown in Paillard et al.<sup>26</sup>). Future research might explore in further detail the relationship between motion sickness and olfaction through the lifespan. Lastly, the olfactory sensitivity to n-butanol has been used in our study. Even if this test has been widely used and was very useful for this study, a larger panel of smells would be interesting to use for the olfactory detection test.

Some authors suggested that unpleasant odors could contribute to motion sickness.<sup>10,13,34</sup> However, Paillard et al.<sup>25</sup> highlighted the lack of influence of odors in motion-induced sickness, but an impact of a nauseogenic test on olfactory perception. Our study delves further into the knowledge of the relationship between motion sickness susceptibility and olfaction by showing some differences in olfactory perception, at both subjective (odor quality rating) and objective (electrodermal measurement) levels, between motion sick and not-motion subjects.

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