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Induction of nocebo effects by verbal suggestions during the caloric test

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Induction of Nocebo Effects by Verbal Suggestions During the Caloric Test

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Abstract

The caloric test is the most frequently performed vestibular diagnostic test and is considered the "gold-standard" for the assessment of the peripheral vestibular system. Using a warm or cool stimulus, the caloric test alters the temperature gradient in the vestibular system resulting in nausea and dizziness. The nocebo effect is a phenomenon that can occur when negative expectations result in negative effects. No study has examined whether expectations of nausea and dizziness during the caloric test enhance the experience of unwanted symptoms. The purpose of this investigation was to determine whether a nocebo response can be elicited during the caloric test. Fifty-four participants between the ages of 18-26 were randomly separated into two groups: one group received positive instructions prior to a modified-caloric test and the other group received negative instructions. Participants then underwent a modified-caloric test with water set to 37 degrees Celsius and not expected to stimulate the vestibular system. Eye movements were recorded using the ICS Chartr 200 videonystagmography system. Physiologic variables included measurements of skin conductance and skin resistance using a GSR Shimmer unit. Subjective variables included a yes/no question about the presence of vertigo, a 7-point severity of nausea rating, and a 20-point motion sickness scale. Covariates included self-report State Trait Anxiety and Motion Sickness Susceptibility questionnaires. Average slow phase velocity of eye movements indicated no vestibular stimulation for either group. Self-reported perception of nausea and motion sickness were minimal and did not differ between groups. The negative instruction group yielded additional peaks in skin conductance and dips in skin resistance compared to the positive instruction group, suggesting increases in physiological arousal in the negative

instruction group. Both groups presented with low State Trait Anxiety and Motion Sickness Susceptibility scores. Negative instructions prior to the caloric test did not produce subjective symptoms of nausea or dizziness. However, it does appear that negative instruction may contribute to higher levels of physiologic arousal during testing. Future research should consider allowing participants to first gain experience with caloric testing and sensations of vertigo prior to the experiment to better facilitate the formation of nocebo effects.

Literature Review

Physical symptoms, such as pain or nausea, can be effectively increased through the induction of negative expectations not attributable to a treatment, a phenomenon called the nocebo effect. The nocebo effect is like the placebo effect, commonly known as induction of positive outcomes not attributable to a treatment. However, it can be argued that the nocebo effect is more akin to that of a self-fulfilling prophecy; that is, a belief that a negative event may occur could lead to the occurrence of that negative event (Shelke, Roscoe, Morrow, Colman, Banerjee, and Kirshner, 2008; Colloca and Miller, 2011). In other words, a nocebo response occurs when an individual's negative expectations subsequently lead to negative outcomes (Hahn, 1997). For example, verbal suggestions of possible adverse events, such as possible side effects of testing or treatment, can produce negative expectations that contribute to negative outcomes. (Colloca and Miller, 2011). The nocebo effect can manifest as either subjective (i.e. nausea) or objective (i.e. vomiting) reactions to a treatment (Liccardi, Senna, Russo…. Passalacqua, 2004). Some studies suggest that there are measurable neurobiological factors that accompany nocebo responses. Specifically, brain-imaging technology has been able to measure activity during nocebo responses in relation to pain (Enck, Benedetti, and Schedlowski, 2008), giving credence to the notion that nocebo responses have some physiological underpinnings.

Pain is one of the most researched physiological responses with regards to the nocebo effect. These effects are commonly measured in medical settings in combination with physical substances, such as lotions, injections, or electricity (Reicherts, Gerdes, Pauli, & Wieser, 2016). Colloca, Sigaudo, and Benedetti (2008) demonstrated the nocebo

effect using tactile stimuli that varied in intensity of pain. They observed that verbal suggestions of pain resulted in perceived pain by the participants even when the stimulus was non-noxious. Their findings also revealed that during low-intensity noxious stimuli exposure, perceived pain levels were higher when suggestion of pain increase preceded the stimulus (Colloca et al., 2008). Similarly, Colloca and Miller (2011) showed that verbal instructions influenced perception of pain during procedures known to cause pain. Specifically, they studied two groups of pregnant women at term gestation. One group was informed before an epidural injection to expect a painful sensation similar to that of a bee sting, while the other group was told the injection would have numbing effects to make them more comfortable. Although both groups received the same epidural, the women given the gentler description rated pain levels as being significantly lower than did the women given the harsher "bee-sting" description. (Colloca and Miller, 2011). These various studies all reiterate the theory behind the nocebo effect and its physiological properties, particularly in medical settings.

Expectancy appears to play a critical role in nocebo responses. There is a reported relationship between symptom expectancies and the subsequent report of symptoms. Shelke et al. (2008) examined the effects of patient expectancy on chemotherapy-induced nausea. The researchers developed a scale that patients used to rank their believed likelihood of developing chemotherapy-induced nausea. The scale ranged from "very unlikely" to "very likely". The study's findings indicated that patients who thought they were "very likely" to experience nausea were actually five times more likely to develop severe nausea than the patients who ranked at the "very unlikely" end of the scale (Shelke et al., 2008). Similarly, Keshavarz and Hecht (2008), in a study

designed to develop and validate a motion sickness index, found that self-reported motion sickness was affected by the level of expected motion sickness conveyed to participants before a motion-provoking test. These studies demonstrate how patient expectations (that may or may not have been formed through verbal suggestions) can influence patient physiological responses and worsen or induce physical symptoms. Improper formation of patient expectation through instruction can not only lead to illegitimate test results, but also strained doctor-patient relationships (Ren & Xu, 2018).

In vestibular testing, pain itself is not induced like in the studies mentioned previously. However, vertigo, nausea, motion-sickness, and, in some cases, vomiting are possible side effects of some vestibular tests. Patients may come to an appointment expecting a negative experience, but their knowledge and understanding of the diagnostic test will largely come from the clinical audiologist. Patients depend on instructions from the audiologist to form an expectation about caloric testing, as it is often a foreign test to patients. Colloca and Miller suggest that conveying information in either a positive or negative manner can affect the formation of nocebo responses in patients (Colloca and Miller, 2011). Thus, the test instructions given in the caloric test may have a profound influence in the patient's physiologic response to the test.

Although the caloric test is widely used in clinics, there is a paucity of knowledge regarding how best to conduct the test with regards to patient instruction. This is problematic because the test may result in unpleasant side effects including nausea, dizziness, and, in some cases, vomiting. As a result, the test may cause great anxiety and discomfort in patients, which can lead to spurious test results (i.e. anxiety can enhance or suppress the measured response). Anecdotally, we have noticed that patients tolerate the

test and feel less symptomatic if they are instructed regarding what to expect and not simply told "they will be dizzy." Many dizzy patients are extremely fearful of feeling dizzy and having a vertigo attack, and the test can be very scary if they do not understand that this is a normal side-effect, does not last long, and is not indicative of a vertigo attack.

To date, no study has systematically examined whether there is a significant impact of instructions on the test, and if there is an impact, what the appropriate instructions to give patients should include (and not include). One of the most commonly cited pieces of literature regarding the caloric test is the "Background and Technique of Caloric Testing", a book chapter from 1990 found in the Handbook of Balance Function Testing. In this chapter, Jacobson & Newman focus largely on the technical aspects of performing the test. They also include the following:

> It is critically important that the caloric examination be discussed with the patient in detail prior to the initiation of the test. In particular, telling the patient that they will, or may, become 'dizzy' or 'nauseous', or that 'they may vomit' will gain one little and in general will 'program' the patient to expect these unpleasant reactions. (p. 165)

This recommendation is largely based on the vast clinical experience of the authors. There is no evidence given as to why we should say these things, and what we should not say. Further, they hint at the possibility of a nocebo effect from improper patient instructions. Ren and Xu (2018) agree that information regarding testing should be given to the patient in an honest, yet encouraging, manner as to avoid inducing an unwanted nocebo effect (Ren & Xu, 2018). There is no consensus on how to instruct patients to

obtain clean, reliable data, and to ensure the patient does not have an overly negative experience.

The purpose of this project is to investigate experimentally the potential nocebo effect on the most commonly administered vestibular test, the caloric test. We hypothesize that nocebo effects can influence subjective measures of vertigo, nausea, and motion sickness and physiological responses of arousal as a result of positive versus negative expectations manipulated via pre-testing instructions to the patient.

Methods

Participants

Fifty-four participants without any history of vestibular impairment or knowledge of vestibular testing partook in this study. Participants were recruited using flyers, class announcements, word of mouth, and the James Madison University Psychology Participant Pool. Demographic information was collected, including participants' age and sex. Participants were between the ages of 18 and 26, with the mean age being 19.5 years (SD 1.8). Each participant was randomly assigned to one of two experimental groups: a positive instruction group and a negative instruction group. All participants were debriefed at the end of testing.

Procedure

Otoscopy was performed on each participant to ensure a clear ear canal free from cerumen or other abnormalities.

Tympanometry was performed on each participant to ensure an intact tympanic membrane as it is extremely critical that water calorics are not performed if a perforation is present. Participants were required to have a Type A, As, or Ad tympanogram.

Body temperature of each participant was recorded using a forehead thermometer. This was later used as a cross check to monitor participants' average body temperature compared to temperature of the water used in irrigation.

Measurements of skin conductance and skin resistance were recorded from each participant using the Shimmer3 GSR+ Unit. The GSR+ Unit analyzes electrical components of an individual's skin to detect eccrine sweat gland fluctuations. The sweat

gland variations are measured as skin conductivity changes in response to individual psychological status. The sweat gland activity is related directly to the emotional and cognitive activity of an individual at the time of the recording (Kuan, Morris, & Terry, 2016). Studies have shown that these physiologic variables give insight into the intensity of an individual's physical reactions. An increase, or a spike, in skin conductance would indicate elevated levels of perspiration, meaning higher levels of anxiety or arousal in the participant (Kuan et al., 2016). The opposite is true of skin resistance; that is, a decrease in skin resistance would suggest increases in participant sweat gland activity. The Shimmer3 GSR+ Unit was clipped onto a wrist band worn on each participant's right hand and contained two Ag/AgCl electrodes that were Velcro-d around the participant's pointer and middle fingers. One electrode measured skin conductance while the other electrode measured skin resistance. The electrodes were connected to the GSR+ Unit via wire leads. The GSR+ device transmitted data via Bluetooth to the ConsensysPRO software on a nearby computer. The signals were sampled at 1 Hz and measured in micro-Siemens (μS) for skin conductance and kilo-Ohms (kΩ) for skin resistance. Recording of the GSR Shimmer Unit began just before instructions about the test were played for each participant.

Instructions were pre-recorded and played for each participant through the loudspeaker of a nearby computer prior to the caloric irrigation. Group 1 received positively-weighted verbal instructions and Group 2 received negatively-weighted verbal instructions. The positive instructions aimed to create expectations of an easy, comfortable test. On the contrary, the negative instructions aimed to create expectations

of dizziness, vertigo, and nausea in participants. The exact recorded instructions are shown in Tables I and II below.

Table I: Recorded instructions conveyed to Group 1 participants

Positive Instructions
For this part of the test, I am going to place warm water in each of your ears separately. The water will dribble in and out of your ears for 30 seconds. The water will be 11 degrees warmer than you are, so it will feel a bit warm in your ear for the first few seconds. I will catch the water in a basin I am placing beneath your ear so that you do not get wet. The warm water will fool your brain for a short period of time into thinking that your head is moving when it isn't. So, you may have a sensation that your head is moving a little bit. If you have that sensation of movement just know that it is normal and it lasts for about a minute. While I am recording, it is important to keep your eyes open since I am measuring your eyes. During the recording, you and I will have a nice conversation or I will ask you to name some items that begin with different letters of the alphabet. You are in charge here. If for any reason you feel uncomfortable please let me know and I will stop the test.

Table II: Recorded instructions conveyed to Group 2 participants

Negative Instructions
For this part of the test, I am going to irrigate each of your ears with hot water. The water will flow into your outer ear canal and then back out into this dish. It will be noisy like Niagara Falls. The water will stimulate a part of the ear that lets me know how your vestibular system is functioning. The hot water often causes dizziness and vertigo and it is common to feel nauseous. I will have a trashcan nearby in case you feel sick. If at any point during testing you feel uncomfortable, I will stop the test. I will need you to keep your eyes open during the test so that I can record your eye movements with the goggles. The test will last for about two minutes for each ear.

Water caloric testing was conducted using the ICS NCI-480 bithermal water caloric stimulator paired with computer-based ICS Chartr 200 videonystagmography (VNG) system. The nystagmus response to 2 caloric irrigations, one in each ear, was recorded using VNG goggles. During caloric irrigation testing, subjects remained in supine position with the head elevated 30 degrees, as is typical of standard caloric testing. Calibration of the VNG goggles was performed using a light bar before testing began.

Typically, caloric testing is conducted using a water temperature that is considerably warmer (i.e. 44 degrees Celsius) or cooler (i.e. 30 degrees Celsius) than the average body temperature of 37 degrees Celsius. During a traditional test, cool and warm water stimuli are delivered to the external ear canal to radiate a change in the temperature gradient of the inner ear, specifically the horizontal semicircular canal (SCC), on the side

of the irrigated ear. This temperature change causes an excitation or inhibition in the horizontal SCC, thereby sending a signal to the central vestibular system that the head is turning. To compensate for the perceived turning, the vestibular system induces a nystagmus response in the eyes called the vestibulo-ocular reflex (VOR). The VOR is observed and measured by the VNG system and the slow phase velocity (SPV) of the VOR is used to assess vestibular function. That is, the greater the velocity of the observed VOR, the greater the peripheral drive from the vestibular system in the tested ear. As a result of stimulating the vestibular system in one ear, the participant may feel a sense of rotation or vertigo during the test followed by a brief period of nausea.

For purposes of this investigation, we conducted a modified-caloric test using a non-noxious stimulus that will neither excite nor inhibit the vestibular system. That is, we conducted the caloric test using a water stimulus of 37 degrees Celsius, equal to body temperature and not capable of inducing a temperature change in the inner ear. To ensure no vestibular stimulation took place, eye movements were carefully measured using VNG goggles.

Data Analysis

Physiologic outcomes included a descriptive analysis of skin conductance and resistance.

Subjective reports of nausea and vertigo were quantified using validated measures including a single yes/no question asking about the presence or absence of movement/vertigo (Jacobson et al. 2017), subjective report of the severity of nausea (7-point rating scale; Shelke et al. 2008), and the Fast Motion Sickness (FMS) scale (20-

point rating scale; Keshavarz & Hecht, 2011). These measures were collected for each ear, immediately following each irrigation.

Covariates included self-reported State Trait Anxiety (STAI; Spielberger et al. 1983) and motion sickness susceptibility as measured using the Motion Sickness Susceptibility Questionnaire (MSSQ-Short; Golding 2006). STAI measures a person's overall anxiety level. MSSQ-S measures a person's overall susceptibility to motion sickness and nausea. Both measures were collected prior to any testing. STAI and MSSQ-S were chosen as covariates to control for baseline anxiety and motion sickness in participants. We anticipated that a participant's natural susceptibility to anxiety or motion sickness may skew the results. Therefore, we decided to control for these individual differences to try to make the results more interpretable and accurate.

Hypothesis

We expected that Group 2 (negative verbal instruction) would yield higher subjective and physiological responses relating to nausea and vertigo than Group 1 (positive verbal instruction). This result would indicate that type of instruction influences a patient's perception of nausea and vertigo and physiologic experience during the caloric test. It was expected that the results of this study would have immediate clinical implications with regards to how we instruct patients prior to caloric testing.

Results

An independent samples t-test was performed to compare body temperature and nystagmus SPV between groups. Average body temperature was 97.24 degrees Fahrenheit, equal to 36.24 degrees Celsius. Body temperature did not differ between groups and was very close to the 37 degrees Celsius stimulus, as seen in Figure 1. Average SPV during the caloric irrigation was approximately 1 degree per second. This did not differ between groups, and indicated no vestibular stimulation.

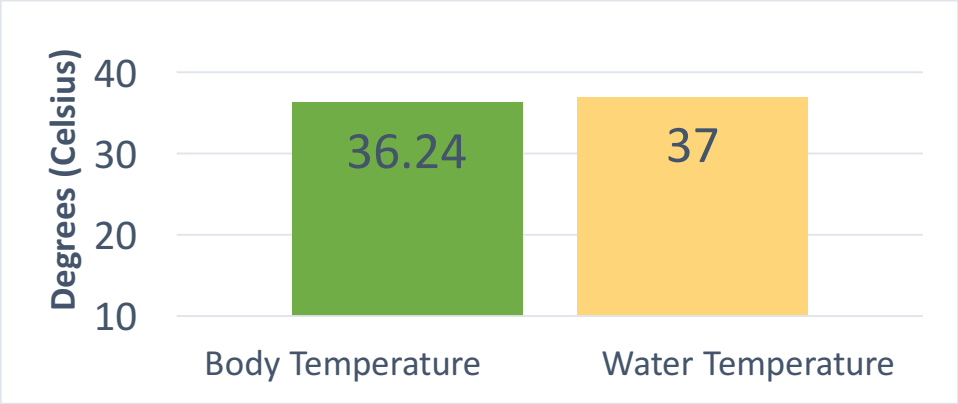

Figure 1. Average body temperature of all participants compared to the water temperature used in this study (in degrees Celsius)

Subjective Outcomes

Participants in both groups reported overall low ratings of nausea and motion sickness, as shown in Figures 2 and 3.

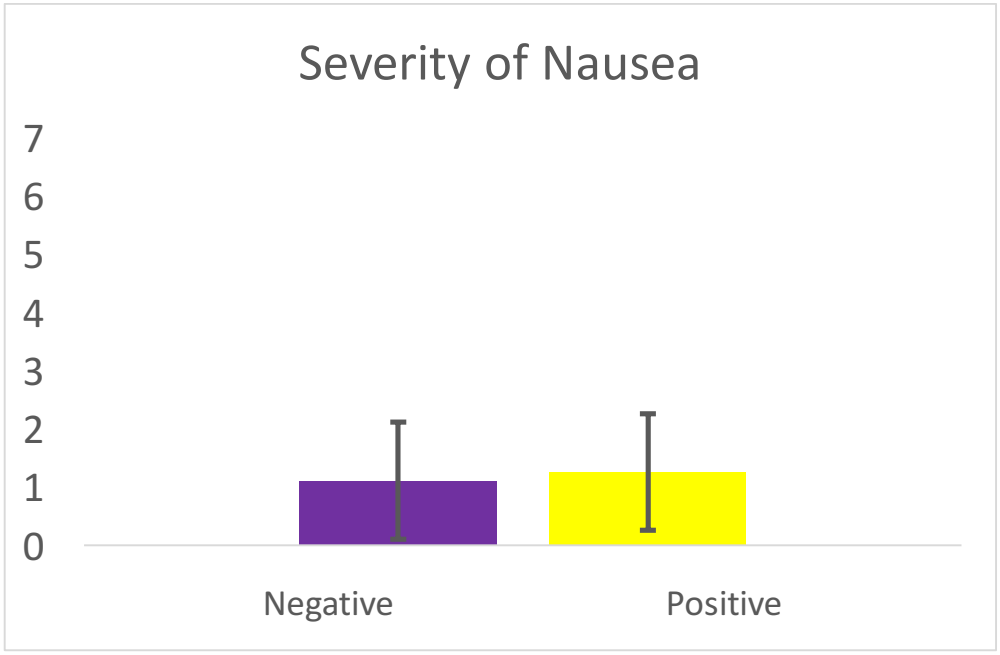

Figure 2. Severity of nausea was reported verbally on a 7-point scale

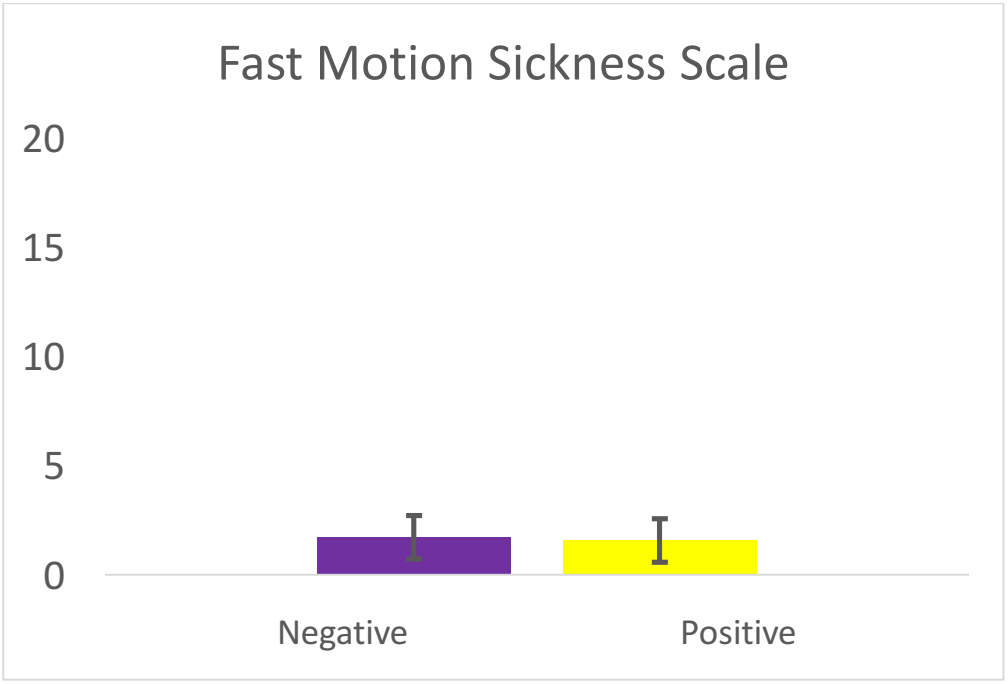

Figure 3. Severity of motion sickness was reported verbally on a 20-point scale

Only 1 participant from each group reported feeling vertiginous during the exam. Therefore, there was not enough data to compute the difference of yes/no presence of vertigo between groups.

An ANCOVA was performed comparing self-report nausea and motion sickness between the two groups using the MSSQ-S and STAI as covariates to control for baseline anxiety and motion sickness. After adjusting for motion sickness susceptibility and state anxiety, there was no statistically significant difference between groups (FMSS, $F = .055$, $p = .815$; severity of nausea, $F = 1.205$, $p = .278$).

Regarding the covariates, previous studies have reported mean MSSQ raw scores of 20, 24, 17, and 19.3. (Brietzke, Klamroth, Dettmann, & Bullinger, 2017; Toschi, Kim, Sclocco, Thurler, Duggento, Barbieri, . . . Napadow, 2016; Iii, 2017; Lamb & Kwok, 2014). The mean MSSQ raw score for our study was 13 (SD 10), considerably lower than average. STAI scores can be classified as "low or no anxiety" (score of 20 – 37), "moderate anxiety" (score of 38 – 44), and "high anxiety" (score of 45 – 80). (Kayikcioglu, Bilgin, Seymenoglu, & Deveci, 2017). The mean STAI score for our study was 31 (SD 7), indicating participants in both groups had low to no anxiety.

Physiologic Outcomes

Skin conductance and skin resistance responses were analyzed by plotting the average values for each group against time in seconds. In this way, changes in physiological arousal are shown as spikes and dips on the graphs and can be descriptively analyzed.

Increases in skin conductance, which correspond to increases in participant perspiration, were marked by peaks in the recording averages. The figures below show the average plotted values with corresponding spikes in skin conduction for the positive group (Figure 4) and the negative group (Figure 5). The recording window shown begins approximately ten seconds before the start of the first caloric irrigation to serve as reference average conductivity. The figures show that the negative group average indicated more peaks than did the positive group average: twenty-four peaks in the former compared to sixteen peaks in the latter.

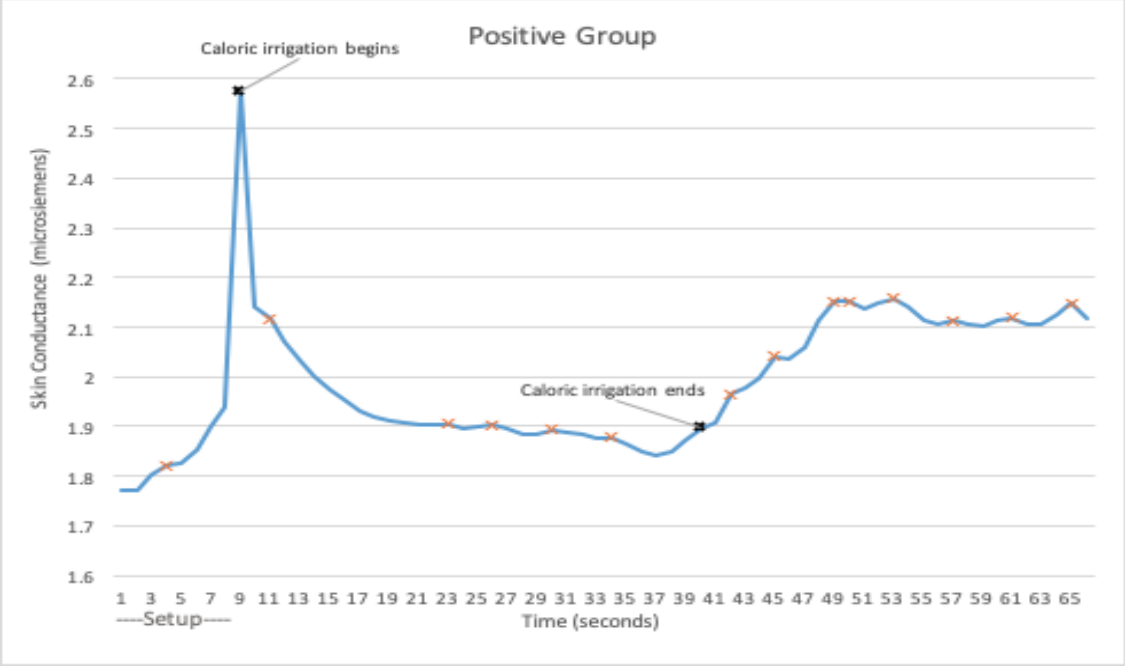

Figure 4. Average skin conductance values (microsiemens) over time (seconds) recorded in the positive instruction group. Peaks in skin conductance are marked with an orange or black X. Black X's indicate the start and end of the first caloric irrigation. 16 total peaks in skin conductance were observed in the positive instruction group.

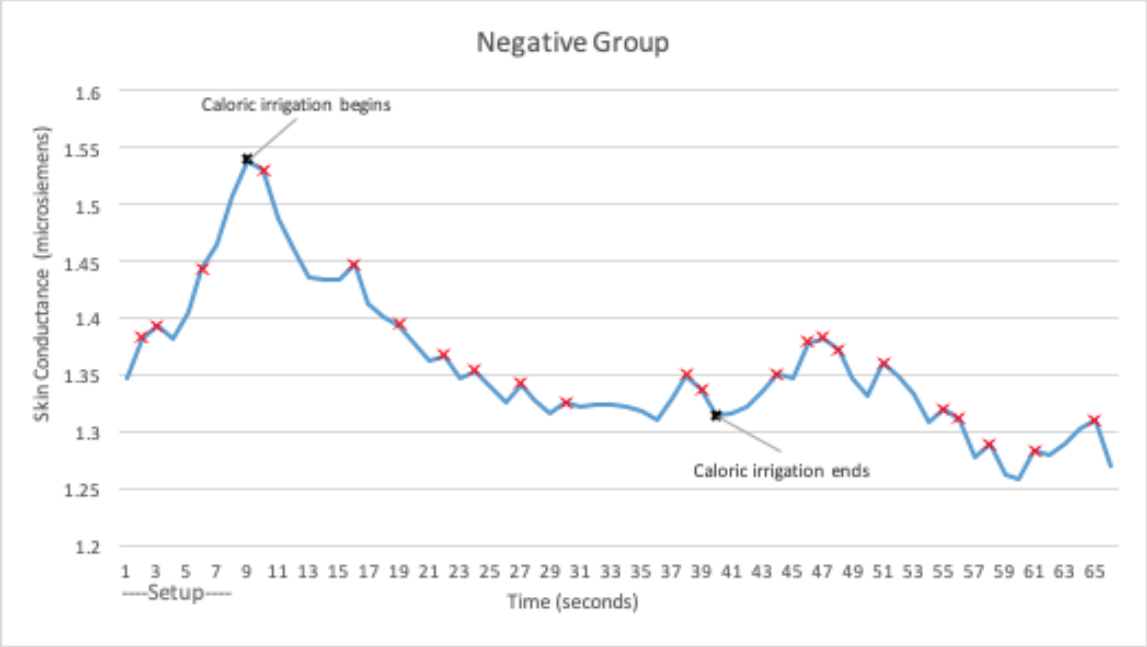

Figure 5. Average skin conductance values (microsiemens) over time (seconds) recorded in the negative instruction group. Peaks in skin conductance are marked with a red or black X. Black X's indicate the start and end of the first caloric irrigation. 24 total peaks in skin conductance were observed in the negative instruction group.

Decreases in skin resistance, which correspond to increases in perspiration, were marked by dips in the recording averages. The figures below show marked dips in the average recordings for both the positive group (Figure 6) and the negative group (Figure 7). Similarly, the negative group indicated more dips than did the positive group. Nineteen dips were marked for the negative group while twelve dips were marked for the positive group.

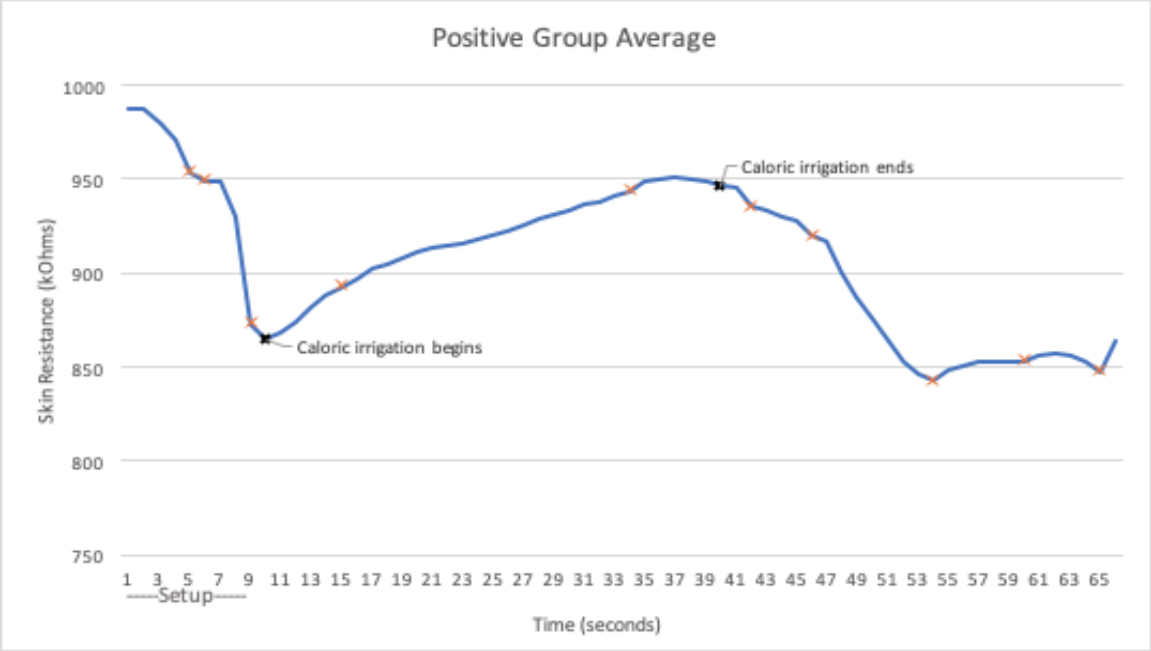

Figure 6. Average skin resistance values (kOhms) over time (seconds) recorded in the positive instruction group. Dips in skin resistance are marked with an orange or black X. Black X's indicate the start and end of the first caloric irrigation. 12 total dips in skin resistance were observed in the positive instruction group.

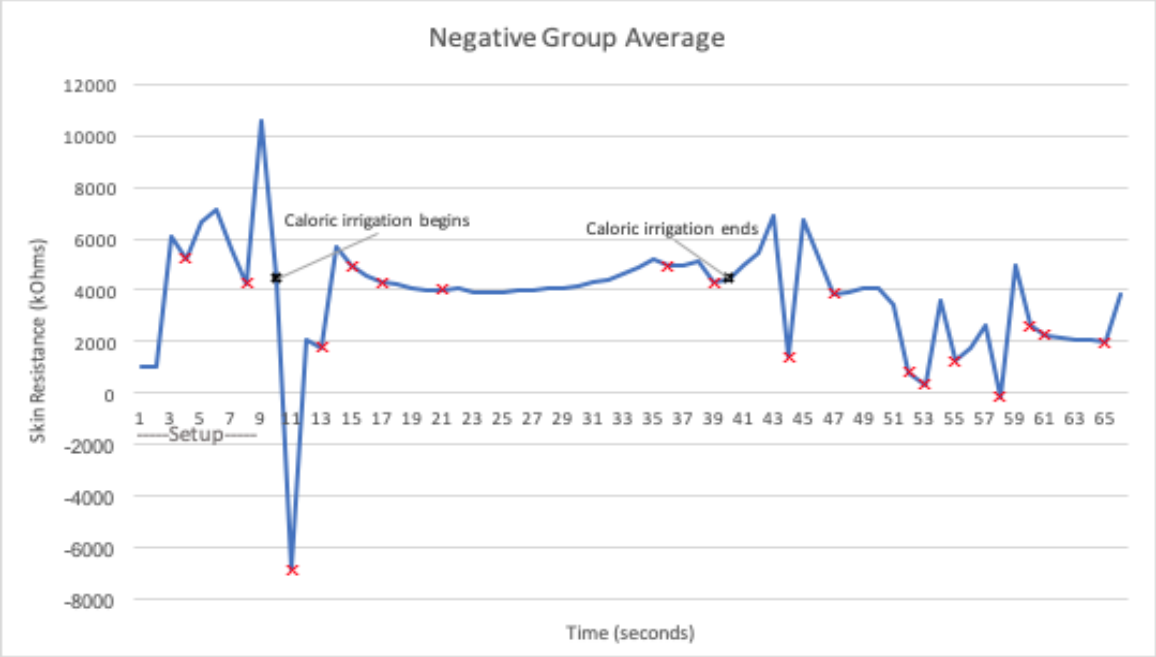

Figure 7. Average skin resistance values (kOhms) over time (seconds) recorded in the negative instruction group. Dips in skin resistance are marked with a red or black

X. Black X's indicate the start and end of the first caloric irrigation. 19 total dips in skin resistance were observed in the negative instruction group.

The results of the Shimmer3 GSR+ Unit recordings of skin conductance and skin resistance demonstrate that the negative instruction group yielded more peaks in skin conductance and more dips in skin resistance than did the positive instruction group, suggesting that spikes in perspiration occurred more often in the negative instruction group.

Discussion

While we were unable to directly induce the nocebo effect in participants in the present study, we did see that arousal levels were increased in the negative instruction group. The overall ratings for nausea and motion sickness were extremely low in both groups. This may be because participants in this study were young, normally-functioning adults, without a history of or experience with vestibular impairment; and individuals are often unaware of their actively-functioning vestibular system until it becomes impaired. The vestibular sensory experience is a largely unconscious experience, and it is difficult to explain vestibular sensation to someone who has never experienced vestibular system impairment.

The nocebo effect occurs when a participant's pre-conceived expectations alter the outcome of an experience (Shelke et al., 2008). Previous studies were able to induce the nocebo effect for events such as pain and nausea using convincing stimuli (i.e. needles and medication), likely because these are commonly experienced events in which participants already have a pre-conceived idea (Shelke et al., 2008; Colloca et al., 2008). Tactile studies assess for the presence of a nocebo effect by telling participants an electric shock will be painful, even if the level of stimulation is known to be non-noxious. In this instance, participants are expecting pain; an electric shock is an understood stimulus. Water-induced vertigo, and consciousness of vestibular sensory function, is not something these participants have ever heard of or experienced. Although participants were told what to expect in the recorded instructions, the participants' naivety to the vestibular system likely contributed to their inability to form true expectations about caloric stimulation. In other words, a strong nocebo effect could not be induced in our

study because the participants had no prior sensation or belief that could be manipulated. The low levels of motion sickness susceptibility and anxiety levels in our participants may have also contributed to the low ratings of nausea and motion sickness.

A study by Reicherts et al. (2016) measured placebo and nocebo responses to visual stimuli that were said to induce pain in a variety of experimental conditions. They found that participant expectations combined with actual experience elicited stronger placebo/nocebo effects through reinforcement. Both experience and expectation together corroborated the suggestion of pain through visual stimuli and resulted in a larger effect. The experience works to reinforce participants' anticipations of what they were told to expect. Additionally, they found that the increase in response was stronger for nocebo effects specifically. The researchers advise that if "weak" nocebo instructions are provided, meaning the plausibility of what participants were told to expect seems strange or less believable (such as the case in water-induced vertigo), the value of the instructions must be reiterated by actual experience (Reicherts et al., 2016). Liccardi et al. (2004) agrees that nocebo effects are more likely to be induced when a participant has already had an unfavorable experience with that particular event (Liccardi et al., 2004).

Perhaps the use of a more provocative stimulus (such as 40 degrees Celsius) performed first would allow participants to gain experience with caloric-induced vertigo. This particular temperature (40 degrees Celsius) would not be warm enough to elicit a clinically-robust response, but it would likely be enough to induce some vestibular stimulation that would create feelings of motion for the participants. Then, the nocebo effect could potentially be induced with further instructions that influence a subsequent caloric irrigation, either positively or negatively. The subsequent irrigation could be a

non-noxious stimulus (37 degrees Celsius, equal to body temperature) as performed in our study. Then, the nocebo effect could be induced in the second irrigation because participants would now have prior sensations and expectations of caloric-induced vertigo from the first irrigation.

Further research into induction of nocebo effects during caloric testing, or other types of vestibular testing, is crucial information needed for clinical audiology. Instructions given to patients before or during testing could potentially make the difference between accurate and inaccurate measurements as well as patient comfort during testing. The implications of this study for additional research regarding psychological impacts of vestibular testing are encouraging and should be explored.

References

Benedetti, F., Lanotte, M., Lopiano, L., & Colloca, L. (2007). When words are painful: Unraveling the mechanisms of the nocebo effect. *Neuroscience,147*(2), 260-271. doi:10.1016/j.neuroscience.2007.02.020

Brietzke, A., Klamroth, A., Dettmann, A., & Bullinger, A. C. (2017). Motion Sickness in Cars: Influencing Human Factors as an Outlook Towards Highly Automated Driving. *Volkswagen*.

Colloca, L., & Miller, F. G. (2011). The Nocebo Effect and Its Relevance for Clinical Practice. *Psychosomatic Medicine,73*(7), 598-603. doi:10.1097/psy.0b013e3182294a50

Colloca, L., Sigaudo, M., & Benedetti, F. (2008). The Role of Learning in Nocebo and Placebo Effects. *Acute Pain,* 211-218. doi:10.1016/j.acpain.2008.05.028

Enck, P., Benedetti, F., & Schedlowski, M. (2008). New Insights into the Placebo and Nocebo Responses. *Neuron,59*(2), 195-206. doi:10.1016/j.neuron.2008.06.030

Hahn, R. A. (1997). The Nocebo Phenomenon: Concept, Evidence, and Implications for Public Health. *Preventive Medicine,26*(5), 607-611. doi:10.1006/pmed.1996.0124

Iii, W. B. (2017). Psychometric evaluation of the Simulator Sickness Questionnaire as a measure of cybersickness. doi:10.31274/etd-180810-5050

Kayikcioglu, O., Bilgin, S., Seymenoglu, G., & Deveci, A. (2017). State and Trait Anxiety Scores of Patients Receiving Intravitreal Injections. *Biomedicine Hub,2*(2), 7-7. doi:10.1159/000478993

Keshavarz, B., & Hecht, H. (2011). Validating an Efficient Method to Quantify Motion Sickness. *Human Factors: The Journal of the Human Factors and Ergonomics Society,53*(4), 415-426. doi:10.1177/0018720811403736

Kuan, G., Morris, T., & Terry, P. (2016). The Use of Galvanic Skin Response (GSR) and Peripheral Temperature (PT) to Monitor Relaxation during Mindfulness Imagery with Relaxing Music. *ASPASP-JPASPEX Special Edition*, *1*(1), 15–21.

Lamb, S., & Kwok, K. C. (2014). MSSQ-Short Norms May Underestimate Highly Susceptible Individuals. *Human Factors: The Journal of the Human Factors and Ergonomics Society,57*(4), 622-633. doi:10.1177/0018720814555862

Liccardi, G., Senna, G., Russo, M., Bonadonna, P., Crivellaro, M., Dama, A., … Passalacqua, G. (2004). Evaluation of the nocebo effect during oral challenge in patients with adverse drug reactions . *J Invest Allergol Clin Immunol*, *14*(2), 104–107.

Reicherts, P., Gerdes, A. B., Pauli, P., & Wieser, M. J. (2016). Psychological Placebo and Nocebo Effects on Pain Rely on Expectation and Previous Experience. *The Journal of Pain*, *17*(2), 203–214. doi: 10.1016/j.jpain.2015.10.010

Ren, Y., & Xu, F. (2018). How patients should be counseled on adverse drug reactions: Avoiding the nocebo effect. *Research in Social and Administrative Pharmacy*, *14*(7), 705. doi: 10.1016/j.sapharm.2018.04.007

Ross, M., & Olson, J. M. (1981). An Expectancy-Attribution Model of the Effects of Placebos. *Psychological Review,88*(5), 408-437. doi:10.1037//0033-295x.88.5.408

Shelke, A. R., Roscoe, J. A., Morrow, G. R., Colman, L. K., Banerjee, T. K., & Kirshner, J. J. (2008). Effect of a Nausea Expectancy Manipulation on Chemotherapy-Induced Nausea: A University of Rochester Cancer Center Community Clinical Oncology Program Study. Journal of Pain and Symptom Management,35(4), 381-387. doi:10.1016/j.jpainsymman.2007.05.008

Toschi, N., Kim, J., Sclocco, R., Thurler, A. H., Duggento, A., Barbieri, R., . . . Napadow, V. (2016). Motion Sickness Increases Functional Connectivity Between Visual Motion and Nausea-Associated Brain Regions. *Gastroenterology,150*(4). doi:10.1016/s0016-5085(16)31820-0