Side Effects May Depend on the Framing of a Warning: But Does this Framing Effect Depend on Absolute Risk?

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Abstract

Side effect warnings contribute directly to the burden of side effects. This occurs via the nocebo effect whereby negative outcomes are shaped by features of the treatment context, beyond the direct actions of the active treatment. Some studies have found that positive framing of warnings – stating the proportion of people who will *not* experience the side effect – reduces side effects compared to the more common-place negative framing – stating the proportion who *will* experience the side effect. However, findings have been mixed. It appears that the absolute risk ascribed to the side effect may determine the effect of framing, however this has not been tested. The current study employed a 2x2+1 between-subjects design to test the impact of both absolute risk and framing of a warning – as well as the inclusion of any statistical warning at all - on side effects. This was done in a model of virtual reality (VR)-induced nausea, with 130 healthy volunteers. Expectancy, anxiety and attentional bias were also measured as they have been proposed as mechanisms of framing and nocebo effects, but scantly - or in the case of attentional bias, never – previously empirically investigated. In this study, VR-induced nausea was not affected by framing or absolute risk of the warning. However, nausea was greater for participants who received no statistical warning. Relative to other groups, these participants also showed elevated anxiety – although not expectancy or attentional bias. These findings indicate that future studies and clinical practices must consider the effects of general, non-statistical warnings on nocebo side effects as they are potentially even more deleterious than more extensive, statistical warnings. These findings are also the first outside of pain studies to support a role for anxiety in nocebo effects, thereby shaping current understanding and future investigations of the poorly understood mechanisms of nocebo effects.

Side Effects May Depend on the Framing of a Warning: But Does this Framing Effect Depend on Absolute Risk?

Merely being warned that a treatment may lead to certain side effects can trigger or exacerbate those effects. These are known as nocebo side effects, in which aspects of the treatment context such as instructions and conditioning by past experiences, rather than the active treatment itself, induce the adverse side effects. The prevalence and burden of nocebo side effects is immense. According to a review by Data-Franco and Berk (2013), up to 74% of patients receiving placebo treatments report side effects. These side effects cannot possibly be due to active treatment as no active treatment is being administered. Beyond being unpleasant in and of themselves, nocebo side effects also lead to treatment non-adherence and additional strain on medical resources (Barsky, Saintford, Rogers, & Borus, 2002). Clearly, warning patients about possible side effects can lead to significant adverse consequences. However, to omit such warnings would pose problems for informed consent. Informed consent serves a number of important purposes, both ethical – protecting patient autonomy – and practical – contributing to legal and administrative compliance (Hall, Prochazka, & Fink, 2012). Thus, warning-induced nocebo side effects create tension between the clinical imperatives to minimise harm and to practice informed consent.

Manipulating the way in which warning information is conveyed provides a promising avenue for balancing these two imperatives. Attribute framing refers to the communication of statistically equivalent risk information in either the positive frame - explicating the chances one will *not* experience the negative outcome - or negative frame - explicating the chances one *will* experience the negative outcome (Barnes et al., 2019). Some studies have found that positive framing of warnings reduces nocebo side effects relative to negative framing (e.g. Faasse, Huynh, Pearson, Colagiuri, & Geers, 2018). However other studies have failed to find this effect (e.g. Caplandies, Colagiuri, Helfer, & Geers, 2017). A potential critical factor

differentiating such studies is the absolute risk of side effects presented. The current study, therefore, sought to determine whether the effect of attribute framing is contingent on the absolute risk of the warned side effect. Furthermore, there is limited evidence that commonly proposed mechanisms of nocebo effects are involved in these framing effects. The current study, therefore, also incorporated measures of expectancy, anxiety, and – for the first time in a nocebo or framing study – attentional bias, as potential mechanisms of any framing effect. The study aimed to shed light on cases in which framing strategies may be usefully deployed in clinical contexts to minimise nocebo side effects, as well as understanding the mechanisms by which these strategies take effect.

The Nocebo Effect

What is the nocebo effect? Nocebo effects occur when supposedly inert elements of a treatment context produce negative outcomes. Nocebo side effects refer to the subset of nocebo effects in which the adverse consequence pertains to a secondary effect, rather than the primary purpose, of the treatment. Nocebo effects are the more sinister counterparts to the better-known placebo effects – in which *benefi*t is derived from supposedly inactive aspects of a treatment context. A variety of triggers – including conditioning procedures and verbal suggestions – have been found to induce nocebo effects.

Nocebo effects can be elicited by instructions alone. Colagiuri, McGuinness, Boakes, and Butow (2012) warned patients undergoing a sham sleep intervention that the treatment may cause changes in appetite. The direction of warnings varied such that some participants were warned that appetite may increase and others were warned that appetite may decrease. Thirty-eight percent of these participants reported a change in appetite, and in all cases, it was in the direction consistent with their warning. That is, patients undergoing the very same inert treatment reported directly opposite adverse effects, depending on the warning they were

given. Nocebo side effects are clearly demonstrated through the production of negative symptoms alongside inert treatments. But perhaps of greater clinical significance, is the occurrence of nocebo effects in conjunction with active treatments. In a double-blind study, Luparello, Leist, Lourie, and Sweet (1970, p. 103) informed asthmatic patients that they were being administered either a bronchodilator – which would make breathing easier - or a bronchoconstrictor – which would make breathing more difficult. In reality, the patient was administered with one of these substances either matching or opposing the information they were given. Bronchoconstriction – as determined by objective measures of lung function – was worse given bronchoconstriction information, compared to bronchodilation information, regardless of which substance was actually administered. This demonstrates the potential of instruction to induce negative symptoms, despite or in concert with, an active treatment.

Nocebo effects can also be elicited by conditioning, in the absence of instructions. For example, Klosterhalfen et al. (2009), repeatedly exposed some participants to a salient oral stimulus soon after a rotation procedure whilst others received equal exposure to the oral stimulus and rotation procedure but the two were not paired. At test, all participants were given the oral stimulus immediately prior to rotation. Those for whom the stimulus had previously been paired with rotation showed lower tolerance for the rotation procedure, demonstrating a nocebo effect triggered by conditioning alone.

Mechanisms of the nocebo effect. As discussed, conditioning and instructions have been shown to generate nocebo effects. As such, conditioning and expectancy – induced by instructions - are often taken to be the mechanisms by which nocebo effects occur. However, this conflates the triggers of nocebo effects, with the psychological processes which underlie them. Elucidation of these psychological processes requires investigation in its own right. Expectancy, anxiety and attentional bias are proposed to be mechanisms of the nocebo effect.

Expectancy. According to Kirsch's response expectancy theory, a person's prediction that they will respond to a stimulus in a particular way is sufficient to produce or enhance that response (Kirsch, 2018). Kirsch suggests that this process of expectation exerts causal influence on one's responses even in the absence of conscious awareness of that expectancy. The contention that one need not be explicitly aware of an expectancy for it to influence their responses complicates empirical investigation of this mechanism. However, Webster, Weinman, and Rubin's (2016) systematic review found that self-reported expectations of symptoms strongly predicted nocebo effects, providing robust evidence of the involvement of this mechanism.

Anxiety. In the context of pain studies, there is evidence that anticipatory anxiety plays a causal role in producing nocebo effects. Colagiuri and Quinn (2018) found that participants in their nocebo hyperalgesia condition reported heightened anticipatory anxiety immediately preceding each pain trial relative to both control and placebo participants. In their study, anticipatory anxiety was measured by self-report and corroborated by skin conductance responses which are a physiological marker of autonomic arousal. Some studies have also found evidence of the involvement of anxiety-related neurochemical pathways in nocebo hyperalgesia. Benedetti, Amanzio, Vighetti, and Asteggiano (2006) found that verbal induction of nocebo hyperalgesia produced hyperactivity of the hypothalamic-pituitary-adrenal axis which is associated with anxiety. Their study further investigated the involvement of anxiogenic neurochemical pathways by administering targeted antagonist drugs. These drugs were able to prevent nocebo hyperalgesia despite having no analgesic effects in the absence of nocebo suggestions. Thus, there is evidence that these anxiogenic neurochemical pathways are not only activated in the case of nocebo hyperalgesia, but are actually essential to eliciting such hyperalgesia. There is some evidence that the specific

mechanisms of nocebo effects depends on the particular outcome at play (Benedetti et al., 2003). As such it is unclear how the role of anxiety generalises beyond hyperalgesia.

Attentional bias. Although theoretical conjecture points to a role for attentional biases, there has not yet been empirical investigation of the involvement of attentional bias in nocebo effects. Colloca and Benedetti (2007) posit that attentional biases are critical in the process by which heightened anxiety leads to nocebo hyperalgesia. They suggest that in cases of hyperalgesia, attention must be focused on the imminent pain, thereby giving way to exacerbated symptoms. Whereas in states of anxious arousal in which attention is focused away from imminent pain, stress-induced analgesic effects may be observed. Research on pain more broadly, provides evidence that increased attention towards particular internal states can exacerbate experiences of symptoms. For example, pain hypervigilance has been found to associate with severity of clinical pain in sufferers of osteoarthritic knee pain (Herbert et al., 2014).

The toll of nocebo side effects. Extricating nocebo-induced side effects from those directly caused by active treatments is difficult, but estimates suggest that nocebo side effects account for 40-100% of drug side effects (Mahr et al., 2017). For example, nocebo side effects appear to contribute strongly to statin intolerance. Statins are a class of drug prescribed to lower cholesterol, and are widely warned to be associated with adverse side effects. Statin intolerance – failure to accept the recommended dose of a statin due to such adverse effects – occurs in an estimated 10% of clinical patients (Tobert & Newman, 2016). However, in double-blind placebo-controlled trials, statin intolerance occurs at roughly equivalent rates between patients receiving statins and placebo. Furthermore, this is still the case when the trials are conducted with patients previously clinically identified as statin-intolerant (Tobert & Newman, 2016), indicating that statin-intolerance is highly unlikely to be a direct result of the

active treatment, but instead, due to nocebo side effects. As such, nocebo side effects exact a significant toll on patients in clinical settings.

Attribute Framing to Mitigate Nocebo Side Effects

Attribute framing effects. Attribute framing refers to the differential presentation of statistical information either in terms of the likelihood of an aversive outcome occurring – the negative frame – or not occurring – the positive frame (Barnes et al., 2019). Tversky and Kahneman (1981) first demonstrated an effect of framing when they provided respondents with forced-choice scenarios which were identical except that they were worded to focus on either lives lost or lives saved. Merely shifting the framing of the question was sufficient to produce a reliable shift in responses.

Framing effects hinge on statistically identical information being evaluated differently. This is consistent with prospect theory as proposed by Kahneman and Tversky (1979). According to this theory, human choice systematically violates the assumptions of objective rationality as it is sensitive to superficial changes in the presentation of information. Of relevance to framing, Tversky and Kahneman (1981) proposed that when possible losses are highlighted, individuals are more prone to taking risks. However, when possible gains are highlighted, individuals are more prone to avoiding risks. Theoretically, this is proposed to be a function of people's propensity to weight gains and losses unequally, even when they are equivalent in absolute value.

Attribute framing in nocebo side effects. In nocebo side effects, the outcome of interest is not a choice – as in Tversky and Kahneman's (1981) forced-choice scenarios - but a symptomatic response. To date, seven studies have been conducted examining the effect of attribute framing on nocebo side effects, and the evidence is mixed. The first study finding evidence of an attribute framing effect was conducted by O'Connor, Pennie, and Dales

(1996), who manipulated side effect warnings for patients receiving influenza vaccinations. Patients were warned about a range of side effects in either the negative frame – e.g. “out of 100 people who get the vaccine, 40 will get a sore arm” – or the positive frame – e.g. “out of 100 people who get the vaccine, 60 remain free of side effects such as a sore arm”. The absolute risk assigned to side effects ranged from 5-40%. For the warned side effects, patients randomly assigned to the positive frame reported lower incidences than those assigned to the negative frame. More recently, Faasse et al. (2018) manipulated side effect warnings for participants ostensibly receiving benzodiazepine tablets but actually ingesting sham tablets. Participants were warned about four side effects which were each assigned a probability between 12% and 31%. Fifteen minutes following ingestion, participants exposed to negatively framed warnings reported greater side effects than those exposed to positively framed warnings, although this framing effect was no longer apparent 24 hours later. Using a model of simulator sickness in virtual reality (VR), Mao (2018) also found that symptoms were less given a positively framed warning compared to a negatively framed or general (no statistic) warning. This study was the first to include a general warning condition, and the results suggested that relative to a general warning, positive framing lessens nocebo side effects whereas negative framing does not seem to alter these effects.

Webster, Weinman, and Rubin (2018) administered sham pills alongside warnings about a range of side effects assigned probabilities of up to 20%. Whilst experiences of symptoms, in terms of number and severity, did not differ between groups, the attribution of these symptoms as drug-related side effects was lower in participants assigned to positive framing. However, interpretation of their results is confounded as the two sets of side effect warnings differed in verbal descriptors of likelihood and form of statistical information (percentages or natural frequencies) as well as attribute framing. These other factors are

considered to modulate framing effects (Barnes et al., 2019) and thus the implications of these findings for attribute framing effects are unclear.

A commonality between the aforementioned framing studies is that the absolute risk assigned to warned side effects is relatively low – never exceeding 40%. In contrast, Caplandies et al. (2017) warned participants about the possible occurrence of headaches as either 70% likely to occur – negative frame – or 30% likely to *not* occur – positive frame - during sham transcranial direct current stimulation. This attribute framing manipulation had no effect on any symptom measures including headache occurrence, frequency or intensity. Likewise, Helfer (2018) found no effect of attribute framing on the percentage of participants reporting headaches in sham transcranial direct current stimulation when headaches were described as a side effect with a 70% chance of occurring. Devlin, Whitford, and Denson (2019) warned participants taking part in a cold pressor task either that "out of 100 people, 20 can leave their hand in longer than 80 s" – positive frame – or "out of every 100 people, 80 are not able to leave their hand in for 80 s" – negative frame. Between framing groups, there were no differences in either discomfort threshold, that is the time at which participants first indicated experiencing discomfort, nor discomfort tolerance, the length of time participants left their hands submerged in the cold pressor.

Comparing these studies, it appears that absolute risk of side effects may be critical to determining whether attribute framing modulates nocebo side effects. As summarised in Table 1, studies which found no effect of framing have employed higher absolute risks than those which have sucessfully found such effects. However, this potentially critical factor has never previously been manipulated within a framing study. So it is unclear whether these divergent findings are in fact due to differences in absolute risk of warned side effects, or other inconsistencies between studies, such as the paradigms employed. If framing techniques

are to be deployed clinically to mitigate nocebo side effects, it is essential to know which cases their use may be appropriate for.

Table 1

Studies of Attribute Framing Effects on Nocebo Side Effects according to Absolute Risk and Outcome

Study	Absolute Risk of Side Effect(s)	Framing Effect?
Webster et al. (2018)	0.1-20%	Confounded
Mao (2018)	30%	Yes
Faasse et al. (2018)	12-31%	Yes
O'Connor et al. (1996)	5-40%	Yes
Caplandies et al. (2017)	70%	No
Helfer (2018)	70%	No
Devlin et al. (2019)	80%	No

Mechanisms of framing in nocebo side effects. As discussed, expectancy, anxiety and attentional biases are proposed as mechanisms by which nocebo effects arise. They are also considered as candidate mechanisms by which framing effects on nocebo side effects may occur. Given the relative brevity of literature pertaining to framing within nocebo side effects, it is not surprising that little empirical evidence has been accrued with regard to the mechanisms of this more specific effect.

Empirical support for the role of expectancy in producing framing effects is minimal. O'Connor et al. (1996) reported an effect of framing on side effect expectancy such that those exposed to positive framing reported lower expectations of side effects and in turn lower side effects. However in this study, the response scale was described to participants as 0% meaning that "no one has this happen to them" and 100% meaning that "everyone has this happen to them". Likely prompting participants to evaluate the overall probability of the side effect rather than their personal expectation that they would experience it. It is notable that

this measure was impacted by differential framing of statistically identical information, however this does not equate to an effect on expectancy per se. Faasse et al. (2018), Mao (2018) and Devlin et al. (2019) each found no effect of framing on expectancy regardless of whether there was an effect of framing on side effects.

Barnes et al. (2019) proposed that the direct effect of positive framing is to attenuate anticipatory anxiety, which then leads to a decrease in attention towards the relevant noxious symptoms and thereby decreased experience of these symptoms. Two previous framing studies have found no difference in anxiety between warning groups (Webster et al., 2018; Mao, 2018). However in each case only a single-item measure was used. There has not yet been any empirical investigation of the potential role of attentional biases in framing effects on nocebo side effects.

The Effect of Absolute Risk on Framing Effects

While there has been no research on the role of absolute risk in framing for nocebo side effects, absolute value has been found to modulate framing effects in other areas. Janiszewski, Silk, and Cooke (2003) asked participants to evaluate products comprised of two components – one of which was established to be the desirable component. For example, blueberry muffins composed of blueberry and muffin batter in which blueberry was established to be the desirable component. Product composition was described in either a negative frame (e.g. 75% muffin batter) or positive frame (e.g. 25% blueberry). It was found that when the level of the desirable component was favourable, evaluations were better given positive framing. However, when the level of the desirable component was unfavourable, evaluations were better given negative framing. Similar reversals have been found in the context of health behaviours. Rothman, Bartels, Wlaschin, and Salovey (2006) reviewed the effect of gain-framed messages – those that highlight the benefits of engaging in a health behaviour – and loss-framed messages – those that highlight the detriments of *not* engaging in

a health behaviour. The effect of frame was found to depend on the risk associated with the health behaviour. Disease detection behaviours, such as mammograms, were deemed to be risky as they may result in unpleasant outcomes – i.e. detection of disease. These were more effectively promoted by loss-framed messages. Disease prevention behaviours on the other hand, such as using sunscreen, were deemed as low-risk as they are not significantly associated with unpleasant outcomes. These were more effectively promoted by gain-framed messages. As such, it appears that outside of the nocebo effect, absolute value plays an important role in modulating the effects of framing. In particular, that framing effects can reverse when moving from low to high absolute values. If such a reversal of framing effects did apply to nocebo side effects, it would mean that positive framing for highly probable side effects may not only be ineffective, but actively harmful.

The Current Study

Based on the available evidence, absolute risk may be a critical factor in modulating the effect of framing on nocebo side effects. This is of great clinical relevance as it delineates the cases in which positive framing may be employed to mitigate nocebo side effects. However absolute risk has not been manipulated in any previous study of framing in nocebo side effects. The current study therefore tested the effect of positive compared to negative framing at both low (30%) and high (70%) absolute risk levels, using a model of VR-induced nausea. This study also included a group that received no statistical warning in order to gauge the effect of including any such warning and thereby the directionality of framing effects. VR-induced nausea is an excellent model to investigate nocebo and framing effects as it has been found to be malleable to such manipulations (Mao, 2018). Furthermore, this is a mild condition which can be quickly elicited in a laboratory context. Moreover, as the applications of VR technology become increasingly ubiquitous across areas including psychological interventions, workplace training and medicine, there is a growing imperative to understand

and decrease the impacts of side effects which currently serve as a barrier to uptake of this technology (Munafo, Diedrick, & Stoffregen, 2017).

As a secondary aim, the current study also sought to shed light on the mechanisms of nocebo and framing effects. As such, expectancy, anxiety and nausea-related attentional bias were tested. This study was the first to test attentional bias following a nocebo or framing manipulation. Also, it was one of few to investigate the mechanisms of nocebo and framing effects in a model other than hyperalgesia. Thus, not only does this study have important clinical implications for the applications of framing to mitigate nocebo side effects, but it also makes novel contributions to understanding the psychological mechanisms by which nocebo effects, and specifically framing effects, come about.

Based on the prediction that the effect of framing on nocebo side effects depends on absolute risk, the critical hypothesis was that there would be a significant interaction between framing and absolute risk on the primary outcome of VR-induced nausea. This was based on the expectation that positive framing would only reduce VR-induced nausea relative to negative framing at low absolute risk, and would have no – or perhaps even the opposite – effect at high absolute risk. Overall, it was expected that nausea would be greater for those exposed to any statistical warning than controls. As attentional biases, anxiety and expectancies are posited to be mechanisms by which framing modulates nocebo side effects, these outcomes were expected to follow the same between-group pattern as nausea. Due to their proposed mechanistic roles, anxiety and expectancy were also expected to predict subsequent experiences of nausea, although the current study lacked the power to analyse such a relationship involving attentional bias.

Method

Participants

Based on the effect size from Quinn & Colagiuri (2016) – a between-subjects experiment testing the influence of instruction on nausea - it was anticipated that a minimum of 24 participants per group (N = 120) would be required. In total, 142 participants took part in the study. All participants were recruited through SONA, 102 were undergraduate psychology students participating in exchange for course credit. The remaining 40 were reimbursed $20 for their participation. Twelve participants withdrew or were excluded (details below), leaving a final sample of 130 participants (81 female). Exclusion criteria were extensive experience with VR, participation in a highly similar study or medical conditions affecting postural stability or propensity to become nauseous. The final sample ranged in age from 17 to 59 (M = 21.19, SD = 5.098). The study was approved by the University of Sydney Human Research Ethics Committee (Appendix A).

Design

This study ostensibly sought to investigate the effects of motion in VR on spatial ability. However, the true purpose of the study was to determine the effect of attribute framing and absolute risk on nocebo side effects, in a model of VR-induced nausea. The study used a 2x2+1 between-subjects design, as shown in Table 2. Participants were randomly assigned to one of five groups, which varied in the side effect warning they received prior to completing a VR task. The warnings differed in both attribute frame (positive / negative) and absolute risk (low – 30% / high – 70%), in addition to a control group. As such, the five groups were 1) negatively framed high-risk warning, 2) negatively framed low-risk warning, 3) positively framed high-risk warning, 4) positively framed low-risk warning, and 5) no statistical warning. Randomisation was stratified according to gender and past VR experience as past studies have found that simulator sickness is greater in females (Jaeger & Mourant, 2001) and those with no prior experience (Hill & Howarth, 2000). Apart from the warnings, the study was identical for all groups. The dependent variables were self-reported nausea

following VR exposure, nausea-related attentional bias, anxiety and expectancy of experiencing nausea.

Table 2

2x2+1 Experimental Design

		Frame of Warning		
		Negative	Positive	No Framing
Absolute Risk of Warning	High	Negative Frame / High-Risk	Positive Frame / High-Risk	
	Low	Negative Frame / Low-Risk	Positive Frame / Low-Risk	
	No Statistic			Control

Materials and Measures

VR environment. The VR environment was a ruins setting, shown in Figure 1, which had been modified by Mao (2018) to produce mild cybersickness – a condition characterised by nausea. This was achieved through the introduction of unnatural movements by reducing friction and gravity and the modification of visual effects, outlined in Table 3. The environment was displayed on a Steam HTC Vive headset using Unity Version 7 on a connected computer. Participants used a Vive handheld controller to move around the environment.

Figure 1. Screenshot of the ruins VR environment.

Table 3

Visual Effects Modified to Create Nauseating VR Environment

Visual Effect Modified	Resulting Experience for User
Depth of field	Blurred background and decreased ability to focus
Motion blur	Blurred trail of motion following head movements
Grain overlay	Overall degraded quality of visuals

Note: Adapted from Mao, A. (2018). *When words matter: The effect of attribute framing on nocebo side effects* (Unpublished honours thesis). University of Sydney, Australia.

VR task. The VR task consisted of approximately nine minutes of verbal instructions (Appendix J). The first 5 minutes of instructions involved simple movements of the body such as “place both hands on top of your head”. The following 4 minutes involved moving around the virtual environment using the Vive handheld controller, for example “tap the left side of the track-pad”. Following this, participants were instructed to use the handheld controller to move continuously around the VR environment for two minutes.

Nausea warnings. In order to comply with ethical obligations and safe work procedures, all participants had to be warned about potential risks of the VR task. Nausea was

explicitly mentioned in the study advertisement (Appendix B) and participant information sheet (Appendix C). At the time of consent, participants were also verbally instructed to notify the experimenter if they felt they were going to faint or vomit at any time. No further nausea warning was given to control participants. A sheet titled 'Information about Virtual Reality' (Appendix G) contained information about virtual reality in general and its use in the present study. Except for sheets given to control participants, the bottom contained a warning reading "The use of Virtual Reality equipment is safe, but it can produce feelings of nausea, ranging from mild to strong… If you experience any nausea, it will pass soon after you stop the VR experience." Embedded in this statement was statistical information which differed between groups, as shown in Table 4. This warning was verbally repeated immediately prior to commencement of the VR task. Note that the warning intentionally only referred to nausea, rather than cybersickness for two reasons. First, nausea is a key component of cybersickness, and a term presumed to be more familiar and meaningful to participants. Second, to reduce cognitive load and facilitate memory, as past studies have found better recall and stronger nocebo effects in participants warned about a single side effect rather than multiple (Colagiuri et al., 2012).

Simulator sickness questionnaire (SSQ). The SSQ (Appendix F) is a questionnaire developed specifically to quantify experiences of simulator sickness. It contains 16 items derived based on a large data set collected from multiple sites and simulators (Kennedy, Lane, Berbaum, & Lilienthal, 1993). Each item is a symptom or sensation such as "nausea", "sweating" and "burping" which respondents rate in terms of their current experience. The questionnaire is comprised of three scales, of which one is specific to experiences of nausea. These subscales are consistent with the factor structure of the questionnaire (Kennedy et al., 1993). In the current study, participants score on the nausea scale was used to operationalise

their experiences of nausea and is thus the primary outcome. In this study, the response scales were modified to 0-10 with accompanying descriptors ranging from “not at all” to “severely”.

Table 4

Nausea Warnings for Each Group

Group	Framed Warning
Negative Framing / High-Risk	From past experiments we typically find that 7 out of 10 people will experience nausea at a level that bothers them.
Negative Framing / Low-Risk	From past experiments we typically find that 3 out of 10 people will experience nausea at a level that bothers them.
Positive Framing / High-Risk	From past experiments we typically find that 3 out of 10 people will **NOT** experience nausea at a level that bothers them.
Positive Framing / Low-Risk	From past experiments we typically find that 7 out of 10 people will **NOT** experience nausea at a level that bothers them.
Control	Omitted

Short-form state-trait anxiety inventory (STAI-6). The STAI-6 (Appendix I) is a short-form index of state anxiety. This scale demonstrates high concurrent validity compared to the well-validated long-form STAI, as well as sufficient reliability (Cronbach’s $\alpha = 0.82$), and is sensitive to fluctuations in anxiety (Marteau & Bekker, 1992). Items such as “I feel calm” are rated in terms of how the respondent feels “right now, at this moment” on a 1-4 scale with accompanying descriptors ranging from “not at all” to “very much”.

Depression, anxiety and stress scales (DASS-21). The DASS-21 (Appendix F) is a 21-item questionnaire consisting of items pertaining to depression, anxiety and stress (Lovibond & Lovibond, 1995). These scales have been found to have strong reliability (lowest Cronbach’s $\alpha = 0.82$) and validity in large non-clinical samples (Henry & Crawford,

2005). Respondents indicate on a 0-3 scale, described as ranging from “not at all” to “very much or most of the time”, their experience of each item over the last week.

Expectancy. The expectancy response scale was based on O’Connor et al.’s (1996) as this study reported effects of framing on expectancy. However, the phrasing was developed to clearly pertain to participants’ expectation of personally experiencing the side effect rather than the generic probability of that side effect. Participants were asked “how likely do you expect it is that you will experience nausea in this VR session?” Responses were marked on a scale which ranged from 0% to 100% labelled at increments of 10% and with markings at increments of 5% (Appendix I).

Attentional bias. A dot-probe task was developed using Inquisit 5. Stimuli were presented on a Sony Triniton Multiscan G420 CRT monitor. Stimuli were displayed in white on a black background. The screen was at approximately eye level, with participants positioned approximately 50cm back from it. The dot-probe task consisted of 120 trials, with five additional practice trials. On each trial, a fixation point was presented in the centre of the screen, followed by a pair of words – one above and one below where the fixation point had been. The words were presented in lowercase, 5mm tall Arial font, which was positioned 1.5cm from the fixation point as per Sharpe, Johnson, and Dear (2015). Participants were instructed to silently read these words. After 1500 ms the words disappeared, and a p or q – the probe - appeared in the place of one of the words. Participants responded by pressing the corresponding p or q button on a Cedrus RB-540 Response Pad as quickly as possible. It was supposed that if the probe appeared in the visual field to which the participant was already attending, the response would be quicker.

The dot-probe task employed three sets of 10 word-pairs – nausea/neutral, threat/neutral and neutral/neutral (Appendix H). Each word pair included one ‘target’ word.

The target words were the nausea or threat stimuli for these pairs, with targets selected randomly within the neutral/neutral word pairs. The threat/neutral and neutral/neutral word pairs were taken from past studies (Dehghani, Sharpe, & Nicholas, 2003; Keogh, Ellery, Hunt, & Hannent, 2001). Attentional bias towards nausea-related words had never previously been tested and so this set of stimuli needed to be developed. To achieve this, twenty candidate nausea-relevant words were derived from the SSQ (Kennedy et al., 1993) and Nausea Profile (Muth, Stern, Thayer, & Koch, 1996). In a piloting phase, these words, as well as the ten threat words, were rated by 16 respondents for nausea-relatedness, threat and general arousal on 11-point scales (Appendix H). Selection of nausea-relevant stimuli was based on ratings of nausea-relevance as well as considering the symptoms which Mao (2018) found to increase most with exposure to this VR task. The selected words were matched with neutral counterparts based on length, number of syllables and word class. This process of stimuli selection and matching is outlined in Appendix H.

Each word pair appeared 4 times throughout the dot-probe task – twice the probe appeared in the same position as the target word – a congruent trial – and twice the probe appeared in the opposite position to the target word – an incongruent trial. Trials were counterbalanced to control for screen position – above or below the fixation point. Reaction times were recorded for each response. Incorrect responses and reaction times less than 200ms or greater than 1000ms were excluded from further analysis, consistent with previous studies (e.g. Dehghani et al., 2003). For each participant, a ‘congruent’ reaction time was calculated as an average of the two congruent trials for each word pair, and an ‘incongruent’ reaction time was calculated as an average of the two incongruent trials for each word pair. These reaction times were averaged across each set of word pairs, producing a mean congruent and mean incongruent response time for each word set. This procedure is consistent with previous studies such as McGowan, Sharpe, Refshauge, and Nicholas (2009).

Postural stability. Postural stability was measured at the commencement and conclusion of VR exposure using a Wii balance board, connected to an iPhone 4 on which the application *BalanceRite* calculated stability scores (Chiarovano et al., 2015). This measure had previously shown ceiling effects in a similar paradigm (Mao, 2018) and thus no between-group differences were hypothesised. Rather, measures were taken to contribute to the credibility of the study's cover-story. Analysis of these measures is included in Appendix M and not discussed further.

Manipulation check. At the end of the experiment participants completed a manipulation check (Appendix K). Firstly, participants were asked to give a brief answer to "What do you think was the purpose of this experiment?" After this, participants were asked "Do you remember being warned about nausea as a possible side effect of VR?" with response options of yes or no. Participants were then asked to rate their confidence in this answer on a zero to ten scale. Following this, participants were asked to recall the warned statistic if possible. They were given the general statements "X out of ten people will experience nausea at a level that bothers them" and "X out of ten people will **NOT** experience nausea at a level that bothers them" to complete. Finally, participants were asked "How much do the following words relate to how you felt using VR?" The subsequent words were the nausea-related words from the dot-probe task and the matched neutral words. The response scale was zero to ten with accompanying descriptors ranging from "not at all" to "extremely".

Procedure

An overview of the procedure is provided in Figure 2. The study took place in one 1-hour session. Participants were informed about the tasks involved in the study, but led to believe that its primary purpose was to assess the effect of motion on spatial ability within a VR context (as opposed to the effect of warnings on nausea). They were then asked to read

and complete a consent form. Consistent with health and safety requirements, participants were verbally instructed to notify the experimenter if they experienced acute symptoms such as feeling as though they were likely to faint or vomit and were reminded about the experiment's exclusion criteria. Following this, participants completed a demographics form (Appendix E). This form included the information necessary for stratified randomisation, which the experimenter undertook in an adjacent room as participants completed baseline measures, i.e. SSQ, STAI-6 and DASS-21. Participants were then asked to read the 'Information about Virtual Reality' sheet, at the end of which was the warning about nausea (except for controls). The experimenter read this warning aloud as the participants read it silently from the sheet. Participants then completed the dot-probe task. Immediately following this, participants completed the expectancy measure and the STAI-6 again.

At this point, participants were taken to the VR equipment. They were instructed to remove their shoes and their height was measured if it was not already known. After becoming familiar with the Wii balance board and the safety rail around it, baseline measures of postural stability were taken. Following this, the VR equipment was explained to, and set up for, the participants. Once wearing the headset, participants were told to follow the upcoming instructions to the best of their ability and reminded of the nausea warning relevant to their group (except controls). Immediately following this reminder, movement instructions were played to participants. After approximately 5 minutes, participants were given the handheld controller in order to complete the remaining 4 minutes of instructions. The experimenter was present at all times, ensuring participants understood and complied with instructions. At the conclusion of the instructions, participants were told to use the handheld controller to move continuously in the VR environment for a period of 2 minutes. If at any point they failed to move for 10 seconds, they were prompted. After this time, participants were verbally administered the SSQ then repeated the measures of postural stability. The

ruins environment continued to be displayed in the headset throughout this process. The VR headset was then removed and participants replaced their shoes. The manipulation check was then administered and participants were debriefed (Appendix M).

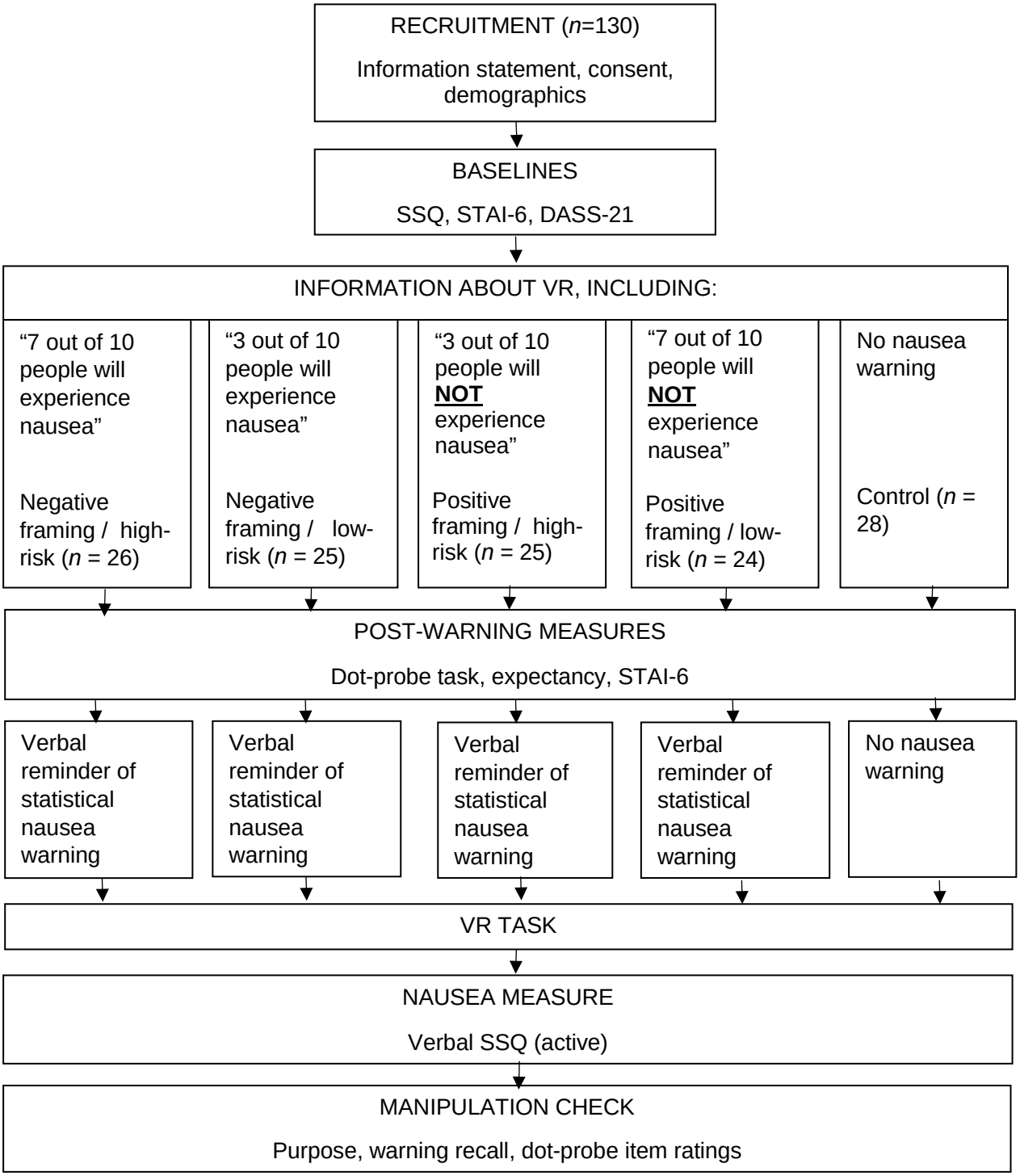

Figure 2. Flowchart of experimental procedure. Excluded and withdrawn participants not shown.

Data Handling and Analyses

All baseline and demographic measures were tested for between-group differences using Chi-Square tests of independence for categorical variables and ANOVAs for continuous variables. If group differences were significant at the $p < 0.1$ level, they were controlled for in subsequent analyses. A between-subjects one-way ANCOVA (5 Levels: negative high-risk warning, negative low-risk warning, positive high-risk warning, positive low-risk warning and control) was performed for the active nausea scale and anxiety, entering the corresponding baseline measures as covariates. A one-way ANOVA (same 5 levels) was performed for expectancy ratings. For each set of results, a set of planned orthogonal contrasts was also run. The first contrast compared the control group to the four framed warning groups. The next three contrasts assessed the 2 (framing) x 2 (absolute risk) component of the study, by testing the main effect of framing, main effect of absolute risk and finally, the interaction effect between framing and absolute risk. This is effectively equivalent to a 2 x 2 ANOVA, but has more power due to inclusion of the control group in the analysis. Hierarchical multiple regression was undertaken to reveal the extent to which anxiety predicted nausea, after entering baseline anxiety and baseline nausea in the first step. Likewise, hierarchical multiple regression was undertaken to reveal the extent to which expectancy predicted nausea, after entering baseline nausea in the first step. For the dot-probe task, a 5 x (2 x 3) ANOVA assessed the influence of group (5), congruence (2) and word type (3) on reaction time. Additionally, an overall attentional bias index was calculated for each set of words (nausea, threat and neutral). These indices were calculated as *mean incongruent response time – mean congruent response time* and compared to zero by single sample t-tests. For all analyses, the threshold of significance was set at $p < 0.05$. Analyses were conducted using IBM SPSS Statistics Version 24.

Results

Baselines

Eight participants withdrew after commencing the experiment, due to feeling unwell whilst completing the VR task. The number of withdrawals did not differ significantly between groups, $\chi 2$ (df = 4, N = 142) = 4.73, p = 0.32. Data from four further participants was excluded. One exclusion was on a priori grounds as the participant had completed a highly similar study in the past. The remaining three exclusions were on ad hoc grounds – two due to technical difficulties, and one due to the participant being unable to understand experimental instructions. The number of exclusions also did not differ significantly between groups, $\chi 2$ (df = 4, N = 142) = 3.35, p = 0.50.

Demographic characteristics for each group are displayed in Table 5. As shown, there were no statistically significant differences between groups in age, gender, VR experience or English language experience. Baseline measures for each group are displayed in Table 6. As shown, there were no statistically significant differences between groups for nausea, STAI-6 or overall DASS-21 scores. Nor were there differences for the depression, anxiety or stress scales of the DASS-21. As no baseline measure reached $p < 0.1$ none were included as covariates in subsequent analysis.

Table 5

Mean and Standard Error for Demographic Factors in each Group and Statistical Test of Between-Group Differences

		Negative Frame / High-Risk	Negative Frame / Low-Risk	Positive Frame / High-Risk	Positive Frame / Low-Risk	Control	Statistical Test
Age	Mean S.E.	21.19 0.60	21.58 0.66	21.00 0.95	20.71 1.01	21.43 1.50	F (4, 125) = 0.11 p = 0.98
Gender	Female Male	17 10	14 12	16 9	16 8	18 10	$\chi 2$ (df = 4, N = 130) = 1.07 p = 0.90
VR Experience	Yes No	14 13	13 13	12 13	14 10	15 13	$\chi 2$ (df = 4, N = 130) = 0.61 p = 0.96
English Language	First Language Not First Language	14 13	16 10	15 10	12 12	15 13	$\chi 2$ (df = 8, N = 130) = 7.57 p = 0.48

Table 6

Mean and Standard Error of Baseline Measures for each Group and Statistical Test of Between-Group Differences

		Negative Frame / High-Risk	Negative Frame / Low-Risk	Positive Frame / High-Risk	Positive Frame / Low-Risk	Control	Statistical Test
Nausea Subscale of the SSQ	Mean S.E.	5.81 0.73	6.19 0.98	4.12 0.67	4.25 0.86	5.00 0.75	F (4, 125) = 1.28 p = 0.28
STAI-6	Mean S.E.	32.96 1.49	32.67 1.88	32.93 1.56	32.40 1.60	31.13 1.21	F (4, 124) = 0.26 p = 0.91
DASS-21	Mean S.E.	23.33 2.47	22.62 2.85	17.52 2.86	18.5 2.87	25.71 3.03	F (4, 125) = 1.48 p = 0.21
Depression Scale of DASS-21	Mean S.E.	6.59 1.09	7.15 1.48	5.44 0.95	4.25 1.01	7.93 1.53	F (4, 125) = 1.31, p = 0.27
Anxiety Scale of DASS-21	Mean S.E.	6.15 1.13	5.77 1.16	5.28 1.30	6.00 0.93	7.29 1.18	F (4, 125) = 0.43, p = 0.79
Stress Scale of DASS-21	Mean S.E.	10.59 1.21	9.69 1.21	6.80 1.14	8.25 1.48	10.50 1.45	F (4, 125) = 1.53, p = 0.20

VR-Induced Nausea

Nausea scores at baseline and at the conclusion of VR exposure (active) are shown in Figure 3. The one-way ANCOVA found no overall statistically significant differences across groups for covariate adjusted mean (M_A) nausea – that is, active nausea controlling for baseline nausea F (4, 124) = 2.286, p = 0.064. Planned orthogonal contrasts, however, revealed higher nausea scores in the control group (M_A = 23.02) compared to the remaining

warning groups on average (M_A = 17.41), F (1, 124) = 4.88, p = 0.03. The remainder of the planned comparisons were not statistically significant, highest F (1, 124) = 2.22, p = 0.14. These results demonstrate an overall effect of an additional, statistical warning on subsequent nausea, in the opposite direction to that predicted. However, no effect of the framing or absolute risk of that warning either directly or through an interaction.

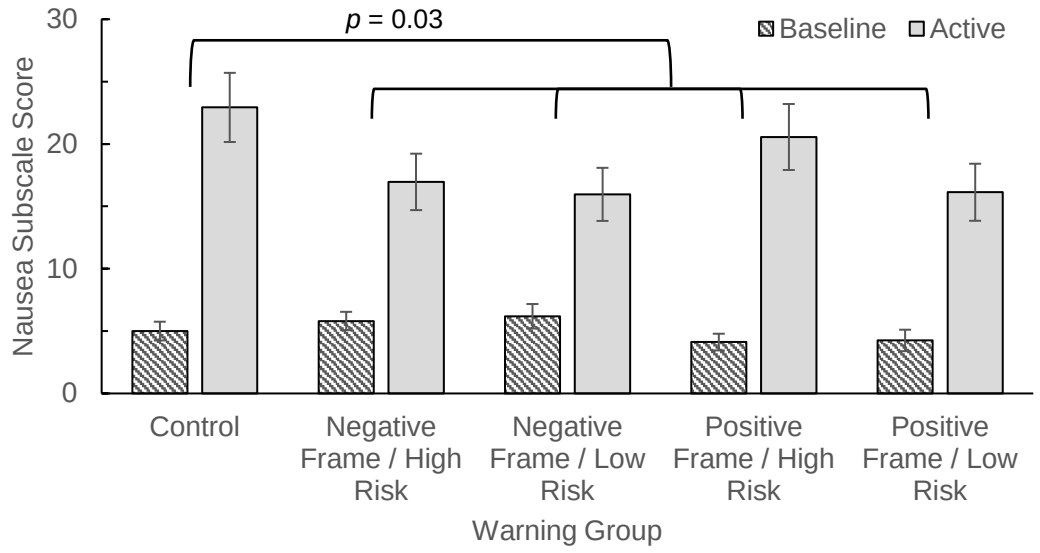

Figure 3. Mean (±SEM) score on the nausea subscale of the SSQ at baseline and following VR exposure (active) for each group.

Expectancy

Expectancy scores are displayed in Figure 4. The one-way ANOVA found no statistically significant differences across groups overall, F (4, 125) = 6.48, p < 0.001. Planned orthogonal contrasts revealed lower expectancy in the control group (M = 23.93) compared to the other groups on average (M = 33.64), t (125) = -2.04, p = 0.04. Also, higher expectancy in the high-risk groups (M = 43.53) compared to the low-risk groups (M = 23.74), averaged over frame, t (125) = 4.47, p < 0.001. Thus, both the addition of a statistical warning beyond control information, and a higher absolute risk in that statistical warning, appeared to

increase expectancies. The remaining contrasts were not statistically significant, highest t (125) = 0.97, p = 0.34. This indicates no effect of framing on expectancy either directly or through interacting with absolute risk.

Hierarchical multiple regression was undertaken to assess the extent to which expectancy predicted nausea. When baseline nausea was entered in the first step and expectancy in the second, expectancy was found to predict an additional 7.1% of variance in active nausea ratings, $R^2_{\text{change}} = 0.07$, F_{change} (1, 127) = 10.66, $p < 0.001$.

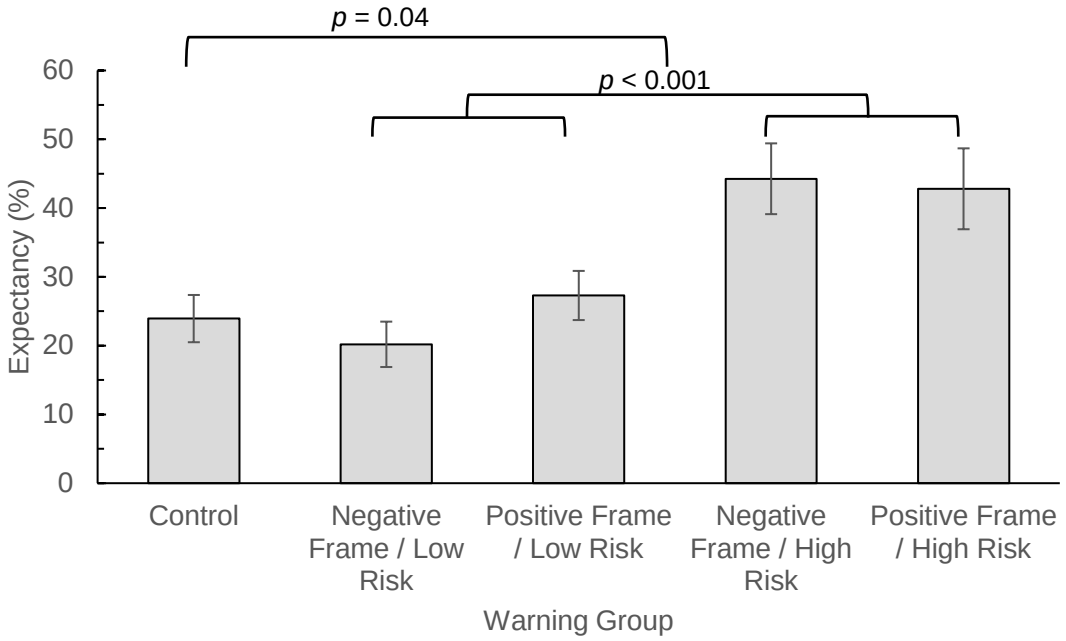

Figure 4. Mean expectancy (±SEM) of experiencing nausea during the VR task for each group, rated as a percentage.

Anxiety

STAI-6 scores at baseline and active measurement are displayed in Figure 5. The one-way ANCOVA found no statistically significant differences across groups overall, F (4, 123) = 1.28, p = 0.28. Planned orthogonal contrasts revealed higher anxiety in the control group (M_A = 35.94) compared to the other groups on average (M_A = 33.04), F (1, 123)= 4.76, p =

0.03. The remaining comparisons were not statistically significant, highest $F = 0.246$, $p = 0.62$. This suggests that receiving any additional statistical warning decreased anxiety relative to only control information, however neither the framing nor absolute risk of the warnings influenced anxiety, directly or through an interaction.

Hierarchical multiple regression revealed that active STAI-6 scores explained 13.2% of variance in active nausea scores, after accounting for baseline nausea and STAI-6 scores (F_{change} (1, 125) = 21.45, $p < 0.001$). A post-hoc paired samples t-test to investigate the overall trend in anxiety scores revealed that averaged across groups, active STAI-6 scores (M = 33.64) were greater than baseline STAI-6 scores (M = 32.42), t (128) = -2.24, p = 0.03.

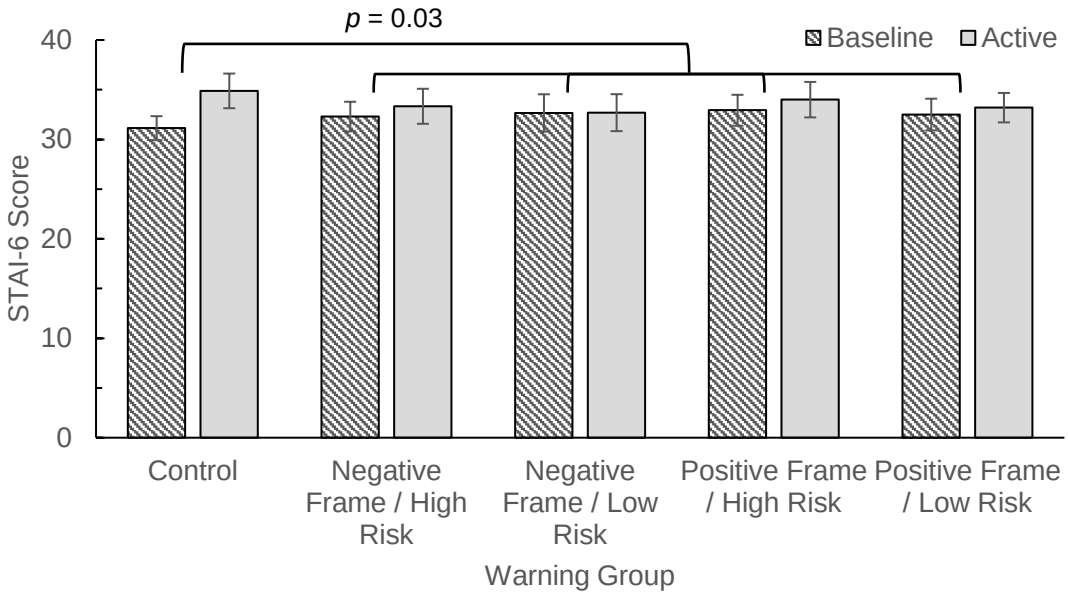

Figure 5. Mean STAI-6 scores (±SEM) at baseline and active measurement for each group.

Attentional Bias

Response times for the dot-probe task are displayed in Table 7. Incorrect responses accounted for 6% of responses overall, these were removed and not further considered. The 5 x (2 x 3) ANOVA revealed a statistically significant main effect of word type on response time, F (2, 250) = 3.457, p = 0.03. No other main or interaction effects were statistically

significant, highest F (1, 125) = 1.28, p = 0.26. Thus it appeared that response time was affected only by the valence of word pairs but not the position of the target word relative to the probe nor the participants' group membership. Pairwise comparisons between nausea, threat and neutral word pairs, revealed that reaction times were greater for nausea word pairs (M = 451) compared to neutral word pairs (M = 448) averaged over group and congruence, p = 0.03, as shown in Figure 6. That is, the appearance of nausea-relevant stimuli slowed responses to the subsequent probe, relative to trials in which only neutral stimuli appeared. No other pairwise comparisons were statistically significant, lowest p = 0.1.

To assess attentional bias within each of the three sets of words, a t-test was run comparing the attentional bias index to zero. For nausea, threat and neutral word pairs, this index did not significantly differ from zero, t (129) = -0.94, p = 0.35, t (129) = -0.67, p = 0.50 and t (129) = -0.40, p = 0.68 (respectively). This suggests that within each word set, attention was not systematically allocated differently between the target words and their neutral pairs.

Sensitivity analysis was undertaken to check whether task-relevant attentional biases may have been present – and potentially contributing to nocebo side effects - but not detected due to the inclusion of additional unrelated nausea stimuli. To achieve this, the above analysis was repeated including only the five nausea words rated as most related to the VR-task in the manipulation check (see below). This analysis yielded no significant results, including no effect of word type (Appendix M).

Table 7

Mean Response Times (ms) and Standard Errors for the Dot-Probe Task According to Valence of the Word Pair and Congruence of the Probe Relative to the Target Word. Data is presented for Each Group and Averaged over Groups (Total).

		Nausea		Threat		Neutral	
		Congruent	Incongruent	Congruent	Incongruent	Congruent	Incongruent
Control	Mean	472.21	469.49	473.19	468.28	472.84	463.67
	S.E.	23.47	21.20	23.03	22.49	21.65	20.60
Negative / High-Risk	Mean	446.53	442.64	441.51	444.78	438.14	441.55
	S.E.	16.99	15.87	14.83	16.19	14.21	15.39
Negative / Low-Risk	Mean	454.49	451.06	451.25	452.61	451.33	447.81
	S.E.	15.43	17.02	15.45	14.84	17.58	15.02
Positive / High-Risk	Mean	442.75	437.93	436.19	432.91	431.19	430.35
	S.E.	13.24	13.40	12.31	12.00	10.95	10.90
Positive / Low-Risk	Mean	440.68	444.98	445.34	440.10	437.79	443.44
	S.E.	15.37	15.59	13.86	14.66	14.25	13.39
Total	Mean	451.85	449.63	449.96	448.26	446.85	445.76
	S.E.	7.84	7.58	7.45	7.46	7.37	6.99

Figure 6. Overall mean response times (ms) (±SEM) for probes presented following nausea, threat or neutral word pairs and either in the same location as the target word (congruent) or the opposite location (incongruent).

Manipulation Check

Purpose of the study. Virtually all participants reported a perception of the purpose of the study that did not suggest awareness of the true purpose. The only exception was one participant who had received a negatively framed, high-risk warning.

Recall accuracy. Between the four groups that received a statistical warning about nausea, recall accuracy differed significantly, $\chi 2 = 10.71$ ($df = 4$, $n = 102$), $p = 0.01$. Hierarchical logistic regression was undertaken, entering frame and risk in the first step and an interaction term in the second. This analysis revealed warning frame as a statistically significant predictor of recall accuracy (Wald = 7.09, $p = 0.01$) such that correct recall was greater given negative (96%) compared to positive (76%) framing. Neither absolute risk nor an interaction between risk and frame was a statistically significant predictor of recall accuracy, highest Wald = 0.007, $p = 0.932$. Post hoc analysis of the primary outcome – VR-

induced nausea – was run excluding participants who failed to accurately recall their warned statistic, the pattern of results did not change (Appendix M).

Dot-probe items. Given that the nausea word pairs used in the dot-probe task were novel, a paired samples t-test was used to assess participants' ratings of the nausea words and their neutral pairs in terms of relevance to the VR experience in this study. As shown in Figure 7, the nausea words were rated as statistically significantly more relevant (M = 3.46) than the neutral words (*M* = 0.61), *t* (129) = -13.562, *p* < 0.001.

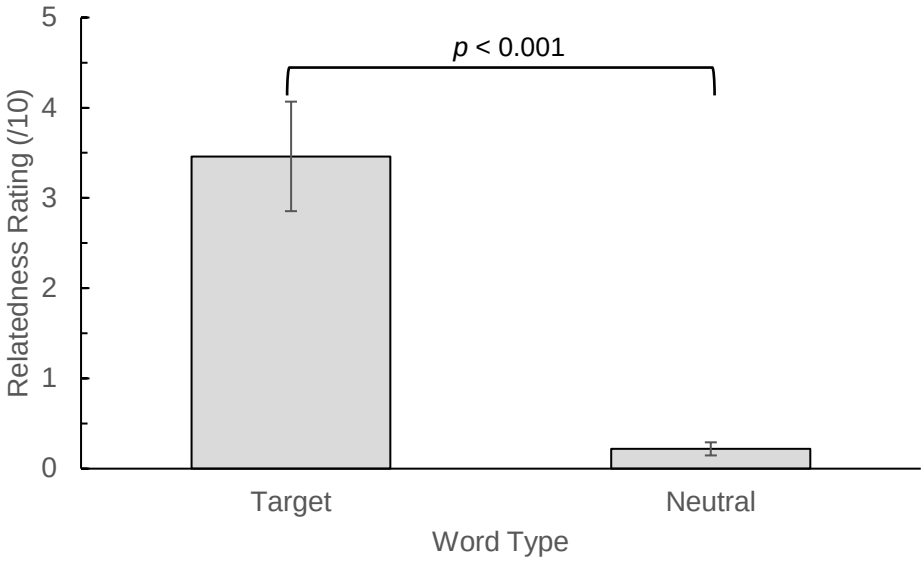

Figure 7. Mean rating (0-10) (±SEM) of nausea stimuli from the dot-probe task (target) and their neutral matched pairs (neutral) for relatedness to the VR experience.

Discussion

The primary aim of the current study was to test – using a model of VR-induced nausea – whether the effect of warning frame on side effect experiences was modulated by the absolute risk conveyed in that warning. Unexpectedly, it was not. In fact, there was no effect of either framing, or absolute risk, or – critically – an interaction between the two, on VR-induced nausea. Opposite to predictions, VR-induced nausea was lower given any additional,

statistical warning, compared to only an initial, non-statistical warning. Although in an unexpected direction, this relative difference in VR-induced nausea is attributable to the only factor differing between groups – the warning procedure – and thus constitutes a nocebo effect. As a secondary aim, this study sought to investigate the roles of anxiety, attentional bias and expectancy as potential mediators of nocebo and framing effects. Notably, the lack of framing effect in this study means that inferences cannot be drawn regarding the mechanisms of framing, but only of nocebo effects more generally. As expected, anxiety was consistent on a group level and predictive on an individual level, of VR-induced nausea, suggesting a mechanistic role. Unexpectedly, nausea-related attentional bias did not correspond with VR-induced nausea. Findings regarding expectancy were less clear, as the between-group pattern of expectancies was incongruent with that of subsequent nausea, but on an individual level expectancy did predict nausea. Recollection of the provided risk information was less accurate following positively, compared to negatively, framed warnings. Although an explicit hypothesis was not made about recollection, this finding is surprising based on previous framing studies. Each of these findings will be discussed in turn.

VR-induced Nausea

Effects of framing and absolute risk on VR-induced nausea. The critical outcome from the current study was the lack of interaction effect between absolute risk and framing of nausea warnings on subsequent experiences of nausea. This was the first study to explore absolute value as a critical factor in framing effects, in the context of nocebo side effects. Contrary to the pattern emerging between previous studies, the current findings do not indicate that absolute risk modulates the effect of framing on nocebo side effects. However, given the absence of an interaction effect to obfuscate a direct effect of framing, it is notable that no framing effect was found either. Past studies employing low-risk warnings have uniformly found that side effects are greater following negatively, compared to positively,

framed warnings (Faasse et al., 2018; O'Connor et al., 1996; Mao, 2018). This was not replicated in the current study. This was clearly not an issue of power as the direction of raw results was such that nausea was marginally greater following positive compared to negative framing in low-risk conditions. Likewise, this does not appear to be attributable to the paradigm employed as the VR task closely matched that used by Mao (2018).

It must be considered that some features particular to the current experimental procedure may have impeded the influence of frame and risk manipulations on nausea. A candidate feature is the inclusion of the dot-probe task following the provision of warnings, which was a key novelty of the current study. The justification for including the dot-probe task was twofold. Firstly, a novel empirical investigation of the proposed role of attentional bias in nocebo and framing effects (Barnes et al., 2019; Colloca & Benedetti, 2007) was considered highly valuable. Secondly, existing evidence suggested that the dot-probe task was a neutral measure. For example, dot-probe tasks are often undertaken between cognitive bias modification procedures and subsequent measures and do not prevent detection of manipulation effects on those measures (e.g. Kakoschke, Kemps, & Tiggemann, 2014). However, these findings do not necessarily translate to the current context as both the manipulations and subsequent measures diverge greatly. By their nature, dot-probe tasks involve exposure to task-relevant stimuli, allowing for the possibility of priming effects – wherein mere exposure to stimuli activates relevant memories and can influence affect and subsequent behaviours (Hermans, Houwer, & Eelen, 1994). In the current study, there was some indication that the dot-probe task exerted a meaningful influence on participants, namely through the elevation of anxiety. Anxiety increased from baseline to active measurement overall, and most markedly so for the control group. Between anxiety measures participants only read information about virtual reality (Appendix G) – which for the control group contained only seemingly benign information – and completed the dot-probe task. The

increase in anxiety cannot definitively be attributed to the dot-probe task, without a comparison group that did not complete it. However, the findings are consistent with this attribution. Thus, the lack of effects, of both framing and absolute risk, could possibly be due to an idiosyncrasy of the current study – namely, inclusion of the dot-probe task.

Whilst it may be that the dot-probe task had a potent influence which interfered with the effects of warning manipulations in the current study, this is far from certain given the current evidence. More generally, the lack of framing effects suggests that framing effects may not be as robust as initial investigations indicated (Barnes et al., 2019). As discussed, the small number of previous framing studies have found mixed results. Whilst disparities in absolute risk were proposed to explain this variation, the current findings instead give credence to the possibility that framing effects may be rather fickle and sensitive to seemingly trivial divergences in experimental procedure. Further studies of framing effects on nocebo side effects are required to elucidate how reliable they are.

The current study does not support the contention that absolute risk determines the effect of warning frame on subsequent side effects. However, this notion should not be conclusively rejected, as it is possible that absolute risk may still play a modulatory role when framing effects are present, which they were not in the current study. The absence of framing effects casts doubt on both the dependability of framing effects themselves and the neutrality of the dot-probe task. The wider implications and directions for further investigation stemming from this will be discussed later.

Effect of any additional, statistical warning on VR-induced nausea. Whilst VR-induced nausea was expected to be lowest in the control group, it was actually observed to be higher in the control group than those that received an additional, statistical warning and subsequent reminder. This is surprising in light of past findings. Past studies have consistently

found that participants that receive no warning about a side effect of interest, experience that side effect less than participants given any framed warning (Helfer, 2018; Caplandies et al., 2017). Mao (2018) ran the only previous framing study to also include groups that received only non-statistical warnings. Mao's (2018) 'no-warning' and 'general warning' groups both received non-statistical nausea warnings. However, in the 'no-warning' group this was limited to brief mentions of nausea in information sheets, prior to distractor tasks. For the 'general warning' group, the extent of warnings was greater, and matched to the framing groups. Whilst nausea was lowest in the 'no-warning' group, in the 'general warning' group it was elevated and equivalent to the negative framing group.

Considering the current results in light of previous findings leads to two notable inferences. Firstly, the current control group and Mao's (2018) 'no-warning' and 'general warning' groups all received non-statistical warnings which led to divergent side effect severities – at least relative to framed information, as direct comparisons have not been made across studies. This demonstrates the variable effects of non-statistical warnings on nocebo side effects. Although, it is not yet clear precisely which aspects of the warning or context determine the extent of these side effects. Secondly, this is the first study in which a *less* extensive side effect warning did not lead to *less* side effects, but in fact *more*. This novel finding demonstrates that it is not universally the case that less mention of a side effect equates to less experience of it, but rather the nature of the warning may be paramount. The wider implications of these findings and directions for future investigation will be discussed later.

Mechanisms of Nocebo Effects

Expectancy. Participants' expectancies of experiencing nausea differed depending on the warning they were given. However, contrary to hypotheses, the between-group pattern of

expectancies did not match that of subsequent nausea. The elevation of expectancy by high-risk compared to low-risk warnings was intuitive, but novel, as the current study was the first to manipulate the absolute risk of side effect warnings. The lower expectancies reported by the control group diverged from Mao's (2018) finding that expectancy did not differ between warning groups – including 'no-warning,' 'general warning' and framed warning groups. This divergence is likely due to some framing groups in the current study receiving high-risk warnings, thereby elevating expectancy in framing groups overall, relative to controls. In comparison, all of Mao's (2018) framing groups received low-risk (30%) warnings. The lack of influence of framing on expectancy in the current study is consistent with previous studies which have found no effect of framing on expectancies, regardless of whether framing impacted on side effects (Devlin et al., 2019; Faasse et al., 2018; Mao, 2018).

Pertinent to the current investigation, there was a clear disjunct between the effect of warning manipulations on expectancy and the effect of the manipulations on experiences of VR-induced nausea. Namely, the control group showed lower expectancy to the other groups, yet conversely, greater nausea and despite the effect of absolute risk on expectancy, there was no such effect on nausea. Overall, whilst these findings uniquely indicate that manipulating aspects of side effect warnings – other than frame – impacts on side effect expectancies, there is no evidence that this mediates an impact of warning manipulations on nocebo side effects.

Expectancy was, however, found to partially predict individual experiences of nausea. Taken alone, the prediction of nausea by expectancy in the current study is consistent with findings in the wider nocebo literature that expectancy strongly predicts side effect experiences (Webster et al., 2016). However, this is seemingly at odds with findings at the group level. One potential explanation is that differential demand characteristics between groups may have driven differences on the group level. Participants recently provided with a relevant statistic may have been compelled to record an answer reflecting that statistic and

thus moderated their responses. Control participants, who had not been provided with a statistic but warned not to take part if they had a propensity to become nauseous, may have been compelled to record lower responses. Thus responses may have been influenced by both genuine expectancies – which in turn influenced nausea – and demand characteristics, based on group membership – which did not. Even if group differences in expectancy reflected a genuine effect of the warning manipulation on participants' expectancies, multiple factors are likely to influence expectancy. Perhaps these multiple components of expectancy differ in their relation to subsequent side effects. The complexities of the relationships between warnings, expectancies and side effects raised in the current study require further interrogation. For instance, consistent with past studies (Devlin et al., 2019; Faasse et al., 2018; Mao, 2018; O'Connor et al., 1996), the current study measured expectancy only once – after the warning manipulation. This limits insight into the various influences on reported expectancies and their relation to subsequent side effects. Future studies may gain further clarity by also measuring expectancy before the relevant warning. However, caution should be taken in not arousing suspicions about the true nature of the experiment.

Anxiety. As hypothesised, the pattern of between-group differences for anxiety matched that of VR-induced nausea, such that both anxiety and nausea were highest in the control group. Furthermore, on an individual level, anxiety partially predicted VR-induced nausea. These results diverged from Mao (2018) and Webster et al.'s (2018) findings that anxiety did not differ between warning groups. This divergence is likely to stem from the use of a more sensitive measure – the STAI-6 – in the current study, compared to single-item scales used in past studies. As discussed, it is postulated that the dot-probe task may have increased anxiety. However, as this task was consistent across groups, it is not thought to explain differences between groups. As mentioned, due to the lack of framing effect on VR-induced nausea, these findings do not offer direct support – or opposition – to the postulation

that anxiety is a mechanism of framing effects (Barnes et al., 2019). However, results do support the role of anxiety in producing nocebo effects more generally. Past studies have found that anxiety plays a causal role in nocebo hyperalgesia (Benedetti et al., 2006; Colagiuri & Quinn, 2018). The current findings extend on this, demonstrating a link between anxiety and nocebo gastro-intestinal symptoms. It should be noted that the current findings do not necessarily demonstrate a *causal* relationship between anxiety and nausea – the warning manipulation could have exerted independent effects on each. However, the contention that anxiety is a causal mechanism of nocebo effects is supported by the current findings – on both group and individual levels – and past investigations which have more explicitly demonstrated causality in a neurochemical study of hyperalgesia (Benedetti et al., 2006). The wider implications of this finding will be discussed in turn.

Attentional bias. Group membership did not impact on nausea-related attentional bias, and therefore, contrary to the hypothesis, the between-group pattern of results for attentional bias did not match that of VR-induced nausea. Regardless of group, there was also no evidence of attentional bias towards or away from nausea stimuli overall, indicating that the warning process did not induce such biases. This was the first nocebo study to empirically investigate attentional bias and findings do not support the contention that attentional bias is a mechanism by which nocebo effects come about (Colloca & Benedetti, 2007). There has been some criticism of the reliability of the dot-probe task, prompting consideration that attentional biases may have been present which were not detected by this measure. However, these criticisms are mainly regarding detection of attentional biases stemming from individual differences rather than experimental manipulations (Schmukle, 2005).

Interestingly, there was a relative delay in responses to nausea compared to neutral word pairs. This delay occurred irrespective of which word the probe appeared in place of, so it was not indicative of an attentional bias but rather a behavioural freezing response.

Behavioural freezing responses have been found, in similar tasks, to occur in the presence of threat, and independently of attentional biases (Clarke, MacLeod, & Guastella, 2013). Notably, this suggests that nausea-related stimuli were appraised as threatening. As the current study was the first to assess nausea-related attentional bias it is unclear whether this results from the experimental context or is a more widely existing reaction to nausea stimuli.

At the conclusion of the study, participants rated the nausea words as more related to the VR task than their neutral pairs, although these ratings were modest overall (M = 3.46 & M = 0.61 out of 10, respectively). This measure was not a reflection of the appropriateness of the stimuli to detect nausea-related attentional biases, especially as the VR task had not yet been experienced at completion of the dot-probe task. Rather, this measure was intended to ascertain the relevance of any attentional biases detected to the treatment at hand. Whilst the significance of this measure was minimal in light of the lack of attentional biases in the current study, it is recommended that future studies examining attentional biases in nocebo side effects also include such a measure.

Recollection of Statistical Risk Information

Participants given a positively framed statistic were less likely to accurately recall that statistic compared to participants warned using a negatively framed statistic. This was unexpected as two previous studies assessed warning recall and did not report any such decrement following positive framing (Mao, 2018; Caplandies et al., 2017). However, the metrics reported by these studies were high recall accuracy overall and no impact of frame on whether participants remembered being given any warning about the side effect of interest. Therefore, the current finding provided the only evidence directly pertaining to the effect of framing on the accurate recollection of risk information. Consistent with past studies, overall accuracy was high (86%), however closer examination revealed it to be much higher

following negative framing (96%) than positive framing (76%). This difference is not negligible and likely to be clinically significant at least in some contexts. It seems that reporting overall accuracy could mask diminished recall following positively framed warnings. Notably, in the current study, all participants who failed to recall the given statistic accurately did not simply fail to provide any statistic, but provided an inaccurate statistic. The wider implications of this finding will be discussed in turn.

Theoretical and Practical Implications

There are a number of important theoretical and practical implications stemming from the current investigation. Firstly, the lack of framing effect on VR-induced nausea either directly or in interaction with absolute value casts doubt on how robust framing effects are. These findings suggest that rather than simply depending on absolute risk, as was hypothesised, framing effects may depend on any number of factors which differ between experiments. This raises questions about the generalisability of framing effects, including to clinical contexts. This is important as interest in framing effects is driven largely by their supposed potential to minimise the harms of nocebo side effects in clinical settings.

Secondly, this study raises important questions regarding the neutrality of the dot-probe task as a measure. This pertains especially to the task's use in the context of framing and nocebo studies – where it had not previously been deployed – but also potentially much more widely. The task is currently assumed to be a neutral measure and as such deployed across a vast array of paradigms. Understanding how this task may affect participants' subsequent experiences and responses is pivotal to interpreting existing results and planning future studies.

Thirdly, whilst previous framing studies employing control groups have uniformly found that *less* warning about a side effect leads to *less* experience of that side effect (Helfer,

2018; Mao, 2018; Caplandies et al., 2017), the current study demonstrates that omission of an additional, statistical warning can, in fact, lead to greater side effects. Particularly in clinical contexts, it is often not viable to include no mention of a potential side effect. The current study demonstrates that, where at least some warning about a potential adverse effect is necessary, a more thorough, statistical warning may actually be preferable – in terms of minimising both nocebo side effects and anxiety – to a brief, general warning. The very divergence of this finding from previous literature demonstrates the heterogeneous effects of fairly similar general warning procedures. This shows that non-statistical warnings should not be considered as unitary comparators for framed warnings, which is an important consideration for study design and interpretation. As non-statistical warnings are common-place in clinical settings, it is of great relevance to understand how they contribute to nocebo side effects, and how this can be minimised.

Fourthly, the current study makes novel contributions to understanding the mechanisms by which nocebo effects are produced, which is of great theoretical value. The current study extends findings that anxiety contributes to nocebo effects beyond hyperalgesia to gastrointestinal symptoms. This gives weight to the contention that anxiety is a mechanism of nocebo effects in general.

Finally, the novel finding that positive, compared to negative, framing produces a decrement in recollection of risk information has significant implications. A key benefit of framing strategies is supposed to be that they may mitigate the burden of nocebo side effects whilst preserving informed consent. Informed consent is compromised if information is provided in a way which is not effectively understood and encoded – or more concerning, which gives way to the encoding of inaccurate information. Thus, doubt is cast on the clinical applicability of framing strategies. As this finding is novel, the full extent of implications are not yet clear. Directions for further research will be discussed later.

Limitations

Despite careful consideration of methodology, this study had limitations. Firstly, it was conducted single-blind such that from randomisation – during the completion of baselines – the experimenter was aware of participants' group membership. This leaves open the possibility that experimenter bias impacted results through the experimenter influencing participants belonging to different groups distinctly. However, it was beyond the scope of the current study to conduct the experiment double-blind and every attempt was made to ensure consistency of experimenter conduct across all participants.

Secondly, there were some limitations stemming from the control warning employed. The control warning used in this study was the minimum required by ethical and safe work standards. This meant it was not possible to include a no-warning control group which would be necessary to gauge the overall nocebo effect as distinct from the effect of the active treatment. Also, in order to make the control warning as minimal as possible, entire nausea warnings – including both statistical and non-statistical statements - were omitted. This means that differences between the control and other groups cannot be definitively attributed to a single feature of the warning process. That is, differences could be due to omission of any additional warnings, of statistical information specifically, or of other specific features of the additional warnings.

Finally, although this study has implications for clinical practice, it was undertaken in a single-session laboratory context. Many contextual divergences may lessen the extent to which findings translate to clinical situations. For example, relevant distinctions are likely to include motivation to engage with warning material, degree of exposure to such material, relationship with the provider, affective state and pre-existing medical conditions. Whilst

again, a clinical study was beyond the scope of the current investigation, it is important to recognise that findings should not be assumed to apply irrespective of context.

Future Directions

Future studies with the scope to do so, should address the aforementioned methodological limitations. In addition there are a number of areas for future investigation illuminated by the current study. Firstly, this study demonstrated the variable and potentially undesirable sequelae of relatively brief, non-statistical side effect warnings. However, it is not yet clear what features of a general warning or its context determine its effect. Future studies should investigate this explicitly, with the view to both inform clinical practice and refine the comparisons drawn between statistical and non-statistical warnings experimentally.

Secondly, future studies should directly assess the neutrality of the dot-probe task. This could be done using a similar experimental design to the present study in which participants are allocated to either complete the dot-probe task, complete a dot-probe task modified to include only neutral stimuli or complete an alternative matched task. This would elucidate whether completion of the dot-probe task in general, or the involved exposure to relevant stimuli in particular, impacts on subsequent measures.

Thirdly, findings from the current study demonstrate the potential for positive framing to impair recollection of risk information. Whilst it has widely been contended that framing strategies preserve informed consent, it seems that this contention has largely been based on assumption and a failure to properly investigate this important factor. It is essential that future studies directly analyse this outcome to determine whether the detrimental effect of positive framing is robust and generalises – particularly to clinical contexts. If this effect does replicate, future research should investigate the potential to mitigate it, and carefully weigh any detriment to recall against other benefits of positively framed warnings.

Finally, the current study sought primarily to determine whether absolute risk of side effect warnings modulates the effect of warning frame. It did not find evidence of such an effect. However, as no framing effect was found either, it remains possible that absolute risk is a moderator of framing effects when they do occur. The imperative remains to clarify this. As such, future framing studies should strongly consider manipulating absolute risk. This may be most effectively done without tests of proposed mechanisms which could potentially interfere with the effects of warning manipulations. Likewise, as no framing effect was observed, evidence was not accrued with regard to the mechanisms of framing. The imperative remains for future studies to investigate this. The measures of anxiety and expectancy employed in the current study detected differences between warning groups which previous studies - employing alternative measures of the same constructs - had not (Devlin et al., 2019; Faasse et al., 2018; Mao, 2018). Thus, future studies should consider use of these instruments in investigating the mechanisms of framing effects.

Conclusions

The current study was the first to investigate whether the effect of warning frame on nocebo side effects depends on absolute risk. This was not found to be the case. However, there was also no effect of framing itself. Whilst this leaves open the possibility that absolute risk modulates framing effects when they do occur, it also casts doubt on how robust these framing effects actually are. If framing effects cannot be reliably elicited in experimental contexts, it is doubtful how effectively they can be generalised across clinical contexts to minimise the immense burden of nocebo side effects. This study also calls into question the widespread supposition that framing strategies do not impair informed consent. Based on the current findings, it is crucial that future studies adequately assess the impact of framing on understanding and recollection of risk information, and that great caution is taken to ensure informed consent is preserved in any clinical applications of positive framing. This was the

first study to show that *less* warning about a side effect can actually lead to *more* experience of that side effect. This provides an early indication that in the countless clinical situations in which at least some mention of a side effect is necessary, providing more extensive, statistical risk information may actually lessen the burden of nocebo side effects. It should be a priority of future studies to clarify the specific features of non-statistical warnings which determine their effect on nocebo side effects. The current study was the first to find evidence supporting a role for anxiety in nocebo effects outside of hyperalgesia. Thus, providing vital support for the proposition that anxiety is a mechanism of nocebo effects in general, and guiding future investigation into the poorly understood mechanisms of nocebo and framing effects.

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Appendices

Appendix A

Ethics Approval

THE UNIVERSITY OF SYDNEY

Research Integrity & Ethics Administration
HUMAN RESEARCH ETHICS COMMITTEE

Thursday, 11 April 2019

[redacted]

[redacted]

Your request to modify this project, which was submitted on 22/03/2019, has been considered.

This project has been approved to proceed with the proposed amendments.

Protocol Number: 2017/971
Protocol Title: The role of instruction and conditioning in VR-induced nausea

Documents Approved:

Date Uploaded	Type	Document Name
22/03/2019	Study Protocol	VR Exp 4b - changes to protocol clean
22/03/2019	Other Type	VR Exp 4b - clean debriefing form
22/03/2019	Advertisements/Flyer	VR Exp 4b - general paid advert clean
22/03/2019	Participant Info Statement	VR Exp 4b - Information Statement Clean
22/03/2019	Advertisements/Flyer	VR Exp 4b - sona paid advert clean
22/03/2019	Advertisements/Flyer	VR Exp 4b - sona psych advert clean

Special Condition/s of Approval

- Thank you for submitting a clear and well supported modification request. Please consider providing debrief and advertisements with version number and date in the footer, to assist any future modifications of these documents. Please contact the ethics office should you require further information.

Sincerely,

[redacted]

Associate Professor Mark Arnold
Chair
Modification Review Committee Chair (MRC 2)

The University of Sydney of Sydney HRECs are constituted and operate in accordance with the National Health and Medical Research Council's (NHMRC) National Statement on Ethical Conduct in Human Research (2007) and the NHMRC's Australian Code for the Responsible Conduct of Research (2007)

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Appendix B

Study Advertisement

How does motion affect our spatial ability in VR settings?

Brief Description: In this study we will be monitoring how the experience of motion affects our ability to perceive aspects of the world presented to us through Virtual Reality (VR) software.

Description: This is a ONE HOUR study, completed in ONE SESSION. During this experiment you will be fitted with a VR headset and will explore VR environments. We will assess your ability to carry out a series of spatial tasks using a Wii Balance Board, as well as asking you to answer some self-report questions of a non-personal nature and complete a computerised attention task.

As a participant, you will be required to attend ONE, SIXTY MINUTE session. It has been found that the VR headset may cause low levels of nausea, but this will disappear once the headset is removed and you have finished the experiment. Your level of motion sickness will be monitored throughout the experiment. We ask that participants do not eat within two hours of attending the study.

We are looking for participants who do not have extensive experience with VR technology (i.e. have used VR no more than 10 times previously). Those who have used VR more than 10 times, who have a medical condition that affects postural stability or increases the risk of nausea, as well as those who are pregnant, are asked not to sign up. This includes those with epilepsy, pacemakers, and pre-existing binocular visual abnormalities. Those who are experiencing inner ear infections and migraines at the time of signing up are also asked not to take part.

Appendix C

Participant Information Statement

THE UNIVERSITY OF SYDNEY

School of Psychology
Faculty of Science

ABN 15 211 513 464

[redacted]

Web: http://www.sydney.edu.au/

How does motion affect our spatial ability in VR settings?

PARTICIPANT INFORMATION STATEMENT

(1) What is this study about?

You are invited to take part in a research study investigating how the experience of motion in Virtual Reality (VR) settings influences our spatial awareness and ability. During this experiment, you will wear a VR headset and will explore VR environments. During this time, we will assess your ability to carry out a series of spatial tasks using a Wii Balance Board as well as asking you to respond to some self-report questions of a non-personal nature. You will also take part in a computerised attention task.

You have been invited to participate because you responded to an advertisement about the study. This Participant Information Statement tells you about the research study. Knowing what is involved will help you decide if you want to take part in the research. Please read this sheet carefully and ask questions about anything that you don't understand or want to know more about.

Participation in this research study is voluntary.

By giving your consent to take part in this study you are telling us that you:

- ✓ Understand what you have read.
- ✓ Agree to take part in the research study as outlined below.
- ✓ Agree to the use of your personal information as described.

You will be given a copy of this Participant Information Statement to keep.

(2) Who is running the study?

The study is being carried out by the following researchers:

[redacted]

This study is being funded by the Australian Research Council.

(3) What will the study involve for me?

If you agree to participate you will be asked to:

[redacted] Attend a single 60-minute session in [redacted]

- ✓ Provide some basic demographic data, e.g. age, gender
- ✓ Complete some basic questions about your current state of well-being
- ✓ Wear a VR headset and explore a series of virtual environments
- ✓ Take part in some spatial tasks that will involve standing on a Wii Balance Board
- ✓ Complete a computerised attention task

(4) How much of my time will the study take?

The study involves one 60-minute session.

(5) Who can take part in the study?

Healthy adults who do not have extensive prior experience with VR (i.e. have used VR no more than 10 times previously). Although the risk to participants is extremely low, those who have a medical condition that affects postural stability or increases the risk of nausea, as well as those who are pregnant, are not eligible to participate in the study.

(6) Do I have to be in the study? Can I withdraw from the study once I've started?

Being in this study is completely voluntary and you do not have to take part. Your decision whether to participate will not affect your current or future relationship with the researchers or anyone else at the University of Sydney.

If you decide to take part in the study and then change your mind later, you are free to withdraw at any time. You can do this by informing the researcher that you wish to withdraw. There will be no negative consequences should you wish to withdraw.

(7) Are there any risks or costs associated with being in the study?

Possible risks may include, but are not limited to:

- ✓ It has been found that, for some, the VR headset may cause low levels of nausea or dizziness, and in very rare cases vomiting. Any experience of this kind will disappear once you finish the experiment and the headset has been removed.

(8) Are there any benefits associated with being in the study?

First year psychology students participating via SONA will receive 1 hour of course credit. All other participants will receive $20 to cover out-of-pocket expenses of their participation.

(9) What will happen to information about me that is collected during the study?

By providing your consent, you are agreeing to us collecting personal information about you for the purposes of this research study. Your information will only be used for the purposes outlined in this Participant Information Statement, unless you consent otherwise.

Your information will be stored securely and your identity/information will be kept strictly confidential, except as required by law. Study findings may be published, but you will not be individually identifiable in these publications.

(10) Can I tell other people about the study?

As prior knowledge of the experimental aims and methods may alter results, it would be appreciated if you could refrain from discussing the experiment with others.

(11) What if I would like further information about the study?

When you have read this information, [redacted] will be available to discuss it with you further and answer any questions you may have. If you would like to

know more at any stage during the study, please feel free to contact [redacted] either via phone [redacted] or email [redacted] or [redacted] via email [redacted]

(12) Will I be told the results of the study?

You have a right to receive feedback about the overall results of this study. You can tell us that you wish to receive feedback by ticking the appropriate box on the Participant Consent From. This feedback will be in the form of a one page lay summary. You will receive this feedback after the study is finished.

(13) What if I have a complaint or any concerns about the study?

Research involving humans in Australia is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this study have been approved by the HREC of the University of Sydney [redacted] As part of this process, we have agreed to carry out the study according to the *National Statement on Ethical Conduct in Human Research (2007).* This statement has been developed to protect people who agree to take part in research studies.

If you are concerned about the way this study is being conducted or you wish to make a complaint to someone independent from the study, please contact the university using the details outlined below. Please quote the study title and protocol number.

The Manager, Ethics Administration, University of Sydney:

- **Telephone:** +61 2 8627 8176
- **Email:** human.ethics@sydney.edu.au
- **Fax:** +61 2 8627 8177 (Facsimile)

This information sheet is for you to keep

Appendix D

Participant Consent Form

THE UNIVERSITY OF SYDNEY

School of Psychology
Faculty of Science

ABN 15 211 513 464

[redacted]

Web: http://www.sydney.edu.au/

PARTICIPANT CONSENT FORM

I, ... [PRINT NAME], agree to take part in this research study.

In giving my consent I state that:

- I understand the purpose of the study, what I will be asked to do, and any risks/benefits involved.
- I have read the Participant Information Statement and have been able to discuss my involvement in the study with the researchers if I wished to do so.
- The researchers have answered any questions that I had about the study and I am happy with the answers.

- I understand that being in this study is completely voluntary and I do not have to take part. My decision whether to be in the study will not affect my relationship with the researchers or anyone else at the University of Sydney now or in the future.

- I understand that I can withdraw from the study at any time.

- I understand that the results of this study may be published, and that publications will not contain my name or any identifiable information about me.

I would like to receive feedback about the overall results of this study YES NO

If you answered **YES**, please indicate your preferred form of feedback and address:

☐ Postal: _____

_____

☐ Email: _____

Please sign below to indicate your consent.

.....

Signature

.....

PRINT name

.....

Date

Appendix E

Demographics Form

Demographic Information

Please answer the questions in the spaces provided. Your answers will remain confidential, only the researchers will have access to this information.

What is your age?

_____

What is your gender?

Female / Male / Other

What is your experience with the English language?

- ☐ English is my first language
- ☐ English is not my first language but it is the main language I speak at home
- ☐ English is not my first language or the main language I speak at home
- ☐ Other: _____

Have you ever experienced Virtual Reality (VR) before?

Yes / No

If yes, how many hours have you spent in Virtual Reality (VR)?

_____

Appendix F

Baselines Form

How does motion affect our spatial ability in VR settings?

How would you rate your overall feeling of wellbeing currently?

Terrible					Fine					Excellent
0	1	2	3	4	5	6	7	8	9	10

You will now be asked about your current experiences of a range of physical symptoms and sensations. Please think carefully about each symptom and ask the experimenter if you are unsure about the meaning of any of the words.

How much are you experiencing each of the following sensations or symptoms currently?

General discomfort

Not at all		Slightly		Mildly	Moderately			Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Fatigue

Not at all		Slightly		Mildly	Moderately			Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Headache

Not at all		Slightly		Mildly	Moderately			Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Eyestrain

Not at all		Slightly		Mildly	Moderately			Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Difficulty Focusing (vision)

Not at all		Slightly		Mildly	Moderately			Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Increased Salivation

Not at all		Slightly		Mildly		Moderately		Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Sweating

Not at all		Slightly		Mildly		Moderately		Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Nausea

Not at all		Slightly		Mildly		Moderately		Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Difficulty Concentrating (mental)

Not at all		Slightly		Mildly		Moderately		Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Fullness of Head (a feeling of pressure in the head)

Not at all		Slightly		Mildly		Moderately		Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Blurred Vision

Not at all		Slightly		Mildly		Moderately		Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Dizzy (Eyes Open)

Not at all		Slightly		Mildly		Moderately		Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Dizzy (Eyes Closed)

Not at all		Slightly		Mildly		Moderately		Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Vertigo (a feeling of being off balance)

Not at all		Slightly		Mildly		Moderately		Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Stomach Awareness (a feeling of discomfort just short of nausea)

Not at all		Slightly		Mildly		Moderately		Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

Burping

Not at all		Slightly		Mildly		Moderately		Strongly		Severely
0	1	2	3	4	5	6	7	8	9	10

A number of statements which people have used to describe themselves are given below. Read each statement and circle the most appropriate number to the right of the statement to indicate how you feel <u>right now, at this moment.</u> *There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.*

	Not at all	Somewhat	Moderately	Very Much
1. I feel calm	1	2	3	4
2. I am tense	1	2	3	4
3. I feel upset	1	2	3	4
4. I am relaxed	1	2	3	4
5. I feel content	1	2	3	4
6. I am worried	1	2	3	4

Please make sure that you have answered *all* of the questions.

Please read each statement and circle a number 0, 1, 2 or 3 which indicates how much the statement applied to you *over the past week*. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

0 Did not apply to me at all
1 Applied to me to some degree, or some of the time
2 Applied to me to a considerable degree, or a good part of time
3 Applied to me very much, or most of the time

1	I found it hard to wind down	0	1	2	3
2	I was aware of dryness of my mouth	0	1	2	3
3	I couldn't seem to experience any positive feeling at all	0	1	2	3
4	I experienced breathing difficulty (eg, excessively rapid breathing, breathlessness in the absence of physical exertion)	0	1	2	3
5	I found it difficult to work up the initiative to do things	0	1	2	3
6	I tended to over-react to situations	0	1	2	3
7	I experienced trembling (eg, in the hands)	0	1	2	3
8	I felt that I was using a lot of nervous energy	0	1	2	3
9	I was worried about situations in which I might panic and make a fool of myself	0	1	2	3
10	I felt that I had nothing to look forward to	0	1	2	3
11	I found myself getting agitated	0	1	2	3
12	I found it difficult to relax	0	1	2	3
13	I felt down-hearted and blue	0	1	2	3
14	I was intolerant of anything that kept me from getting on with what I was doing	0	1	2	3
15	I felt I was close to panic	0	1	2	3
16	I was unable to become enthusiastic about anything	0	1	2	3
17	I felt I wasn't worth much as a person	0	1	2	3
18	I felt that I was rather touchy	0	1	2	3
19	I was aware of the action of my heart in the absence of physical exertion (eg, sense of heart rate increase, heart missing a beat)	0	1	2	3
20	I felt scared without any good reason	0	1	2	3
21	I felt that life was meaningless	0	1	2	3

Appendix G1

Information about VR – Positive Frame / Low-Risk

Information about Virtual Reality

As you understand, we are investigating how motion affects spatial ability in Virtual Reality (VR) settings.

VR is a computer-generated immersive environment that simulates a realistic experience. A person using VR equipment is able to "look around" the artificial world, move around in it, and interact with virtual features or items.

You will be using a headset which is a wearable display that can reflect projected images and allows you to see the virtual environment. Your head movements will be tracked which means that the image in front of you will shift as you look up, down, side to side or angle your head.

You will also be given a handheld unit with a circular track pad to control your movement in the VR environment.

You will be in the VR environment for a total of 10 minutes. However, if at any time you wish to stop the experiment for any reason, please let the experimenter know.

Warning: The use of Virtual Reality equipment is safe, but it can produce feelings of nausea, ranging from mild to strong. From past experiments we typically find that 7 out of 10 people will **NOT** experience nausea at a level that bothers them. If you experience any nausea, it will pass soon after you stop the VR experience.

Appendix G2

Information about VR – Negative Frame / Low-Risk

Information about Virtual Reality

As you understand, we are investigating how motion affects spatial ability in Virtual Reality (VR) settings.

VR is a computer-generated immersive environment that simulates a realistic experience. A person using VR equipment is able to "look around" the artificial world, move around in it, and interact with virtual features or items.

You will be using a headset which is a wearable display that can reflect projected images and allows you to see the virtual environment. Your head movements will be tracked which means that the image in front of you will shift as you look up, down, side to side or angle your head.

You will also be given a handheld unit with a circular track pad to control your movement in the VR environment.

You will be in the VR environment for a total of 10 minutes. However, if at any time you wish to stop the experiment for any reason, please let the experimenter know.

Warning: The use of Virtual Reality equipment is safe, but it can produce feelings of nausea, ranging from mild to strong. From past experiments we typically find that 3 out of 10 people will experience nausea at a level that bothers them. If you experience any nausea, it will pass soon after you stop the VR experience.

Appendix G3

Information about VR – Positive Frame / High-Risk

Information about Virtual Reality

As you understand, we are investigating how motion affects spatial ability in Virtual Reality (VR) settings.

VR is a computer-generated immersive environment that simulates a realistic experience. A person using VR equipment is able to "look around" the artificial world, move around in it, and interact with virtual features or items.

You will be using a headset which is a wearable display that can reflect projected images and allows you to see the virtual environment. Your head movements will be tracked which means that the image in front of you will shift as you look up, down, side to side or angle your head.

You will also be given a handheld unit with a circular track pad to control your movement in the VR environment.

You will be in the VR environment for a total of 10 minutes. However, if at any time you wish to stop the experiment for any reason, please let the experimenter know.

Warning: The use of Virtual Reality equipment is safe, but it can produce feelings of nausea, ranging from mild to strong. From past experiments we typically find that 3 out of 10 people will **NOT** experience nausea at a level that bothers them. If you experience any nausea, it will pass soon after you stop the VR experience.

Appendix G4

Information about VR – Negative Frame / High-Risk

Information about Virtual Reality

As you understand, we are investigating how motion affects spatial ability in Virtual Reality (VR) settings.

VR is a computer-generated immersive environment that simulates a realistic experience. A person using VR equipment is able to “look around” the artificial world, move around in it, and interact with virtual features or items.

You will be using a headset which is a wearable display that can reflect projected images and allows you to see the virtual environment. Your head movements will be tracked which means that the image in front of you will shift as you look up, down, side to side or angle your head.

You will also be given a handheld unit with a circular track pad to control your movement in the VR environment.

You will be in the VR environment for a total of 10 minutes. However, if at any time you wish to stop the experiment for any reason, please let the experimenter know.

Warning: The use of Virtual Reality equipment is safe, but it can produce feelings of nausea, ranging from mild to strong. From past experiments we typically find that 7 out of 10 people will experience nausea at a level that bothers them. If you experience any nausea, it will pass soon after you stop the VR experience.

Appendix G5

Information about VR – Control

Information about Virtual Reality

As you understand, we are investigating how motion affects spatial ability in Virtual Reality (VR) settings.

VR is a computer-generated immersive environment that simulates a realistic experience. A person using VR equipment is able to “look around” the artificial world, move around in it, and interact with virtual features or items.

You will be using a headset which is a wearable display that can reflect projected images and allows you to see the virtual environment. Your head movements will be tracked which means that the image in front of you will shift as you look up, down, side to side or angle your head.

You will also be given a handheld unit with a circular track pad to control your movement in the VR environment.

You will be in the VR environment for a total of 10 minutes. However, if at any time you wish to stop the experiment for any reason, please let the experimenter know.

Appendix H

Development of Dot-Probe Stimuli

Materials for Piloting Potential Dot-Probe Stimuli

Rate each word on the given scales by marking an X at the appropriate point.

Sick

Highly Negative		Highly Positive
Not at all arousing		Highly arousing
Not at all representative of nausea		Highly representative of nausea

Salivation

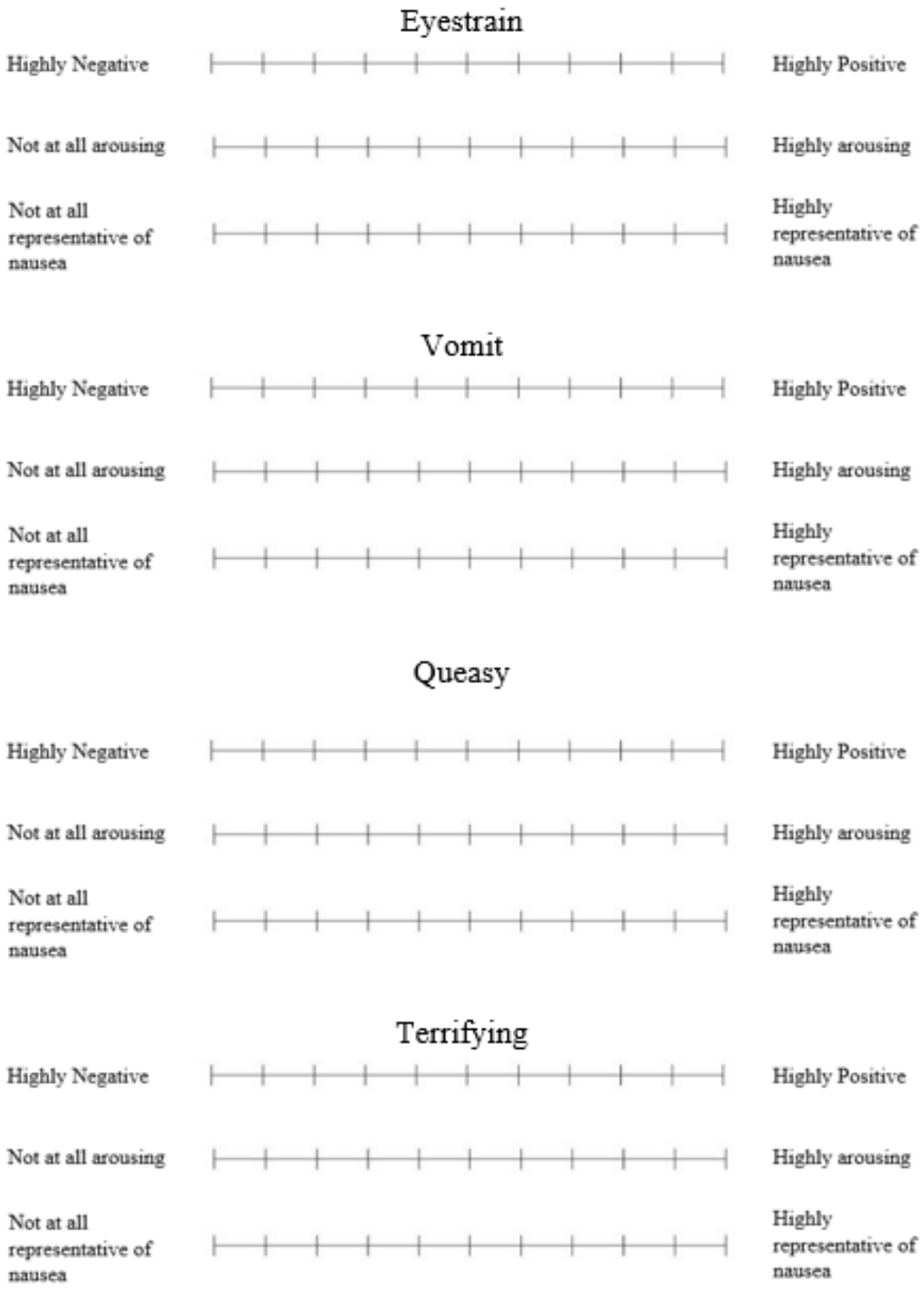
Highly Negative		Highly Positive
Not at all arousing		Highly arousing
Not at all representative of nausea		Highly representative of nausea

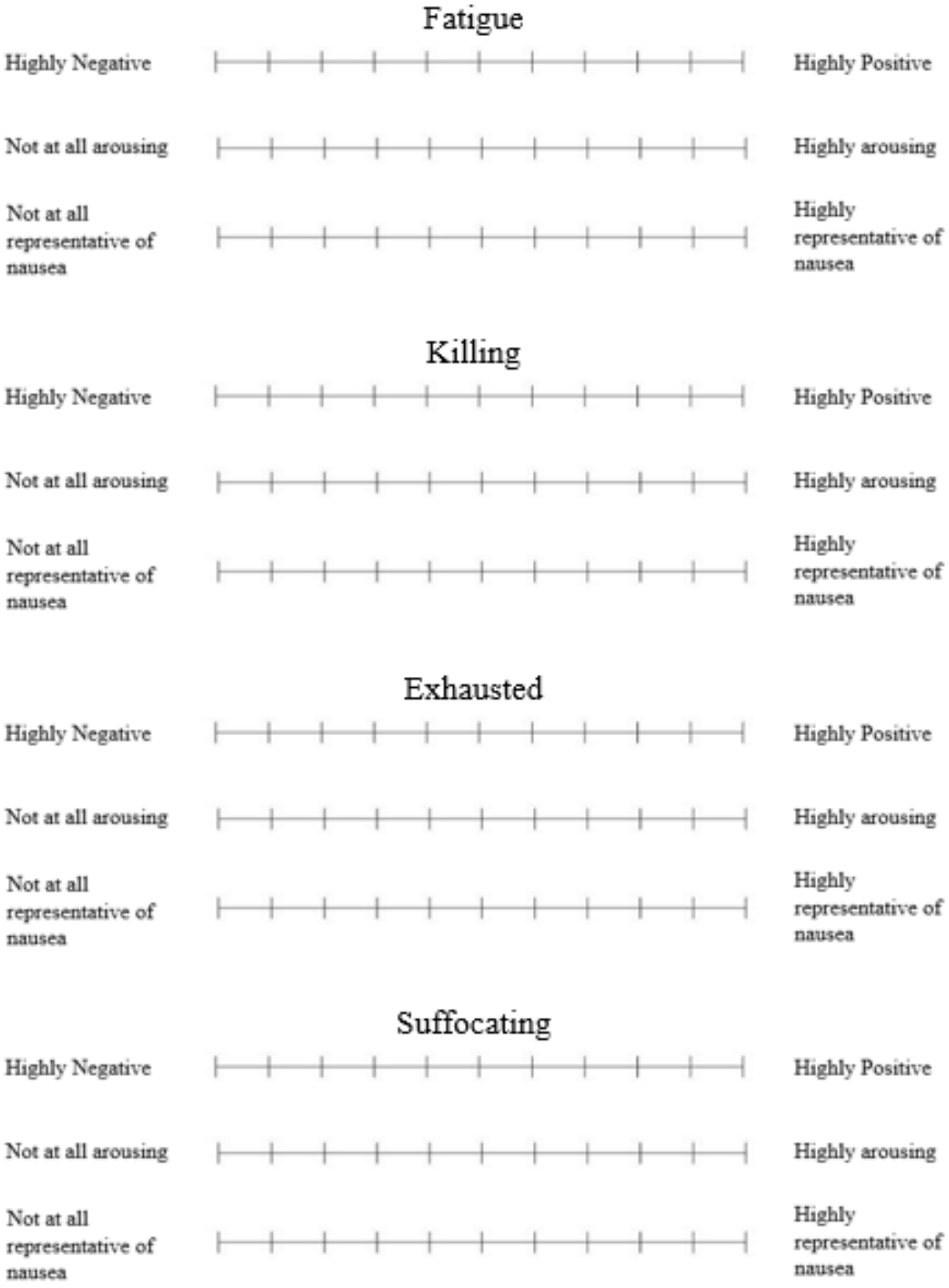
Discomfort

Highly Negative		Highly Positive
Not at all arousing		Highly arousing
Not at all representative of nausea		Highly representative of nausea

Fearful

Highly Negative		Highly Positive
Not at all arousing		Highly arousing
Not at all representative of nausea		Highly representative of nausea


Eyestrain
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Vomit
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Queasy
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Terrifying
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea


Fatigue
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Killing
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Exhausted
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Suffocating
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea

Scared

Highly Negative — Highly Positive

Not at all arousing — Highly arousing

Not at all representative of nausea — Highly representative of nausea

Weak

Highly Negative — Highly Positive

Not at all arousing — Highly arousing

Not at all representative of nausea — Highly representative of nausea

Danger

Highly Negative — Highly Positive

Not at all arousing — Highly arousing

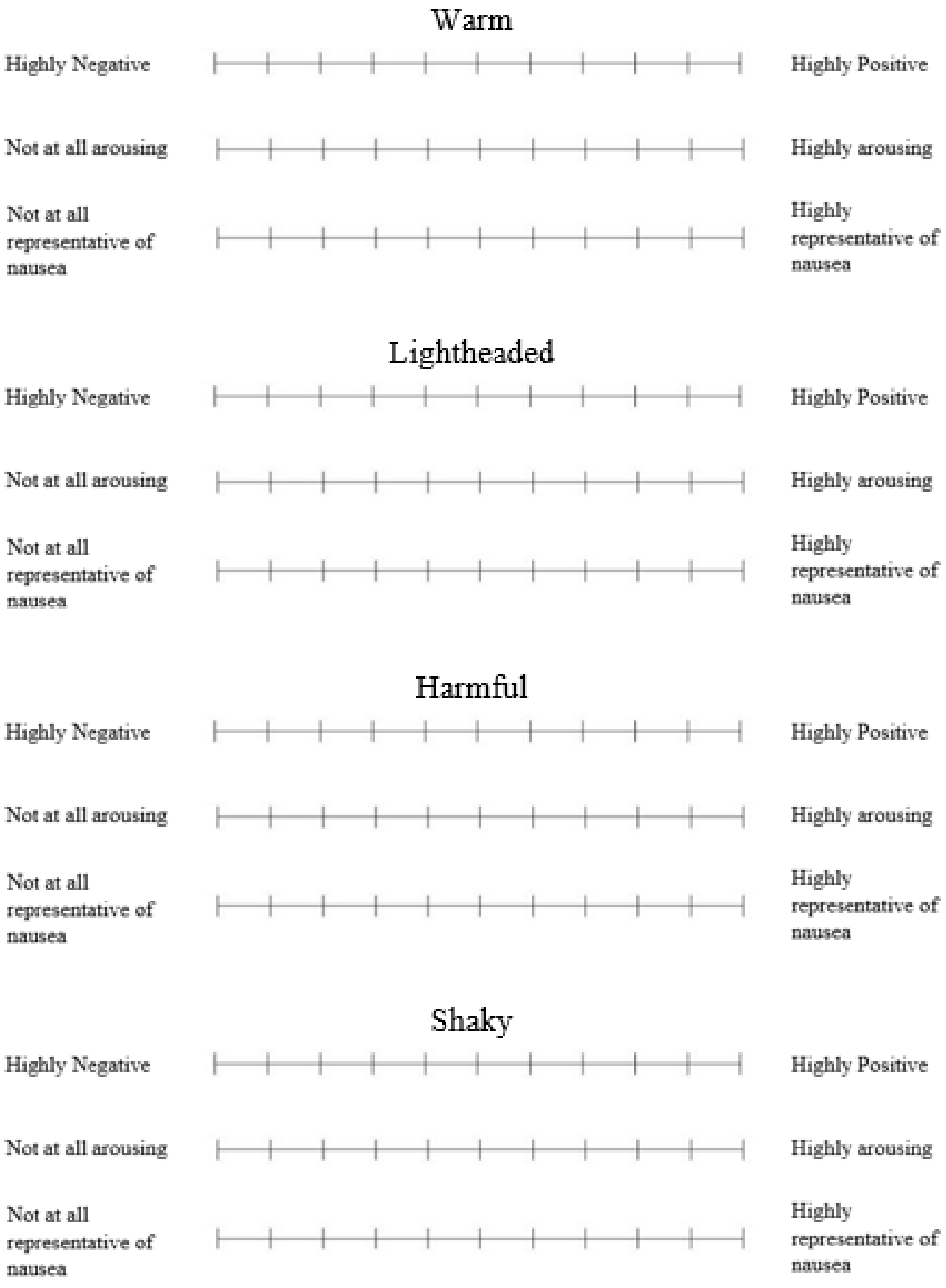
Not at all representative of nausea — Highly representative of nausea

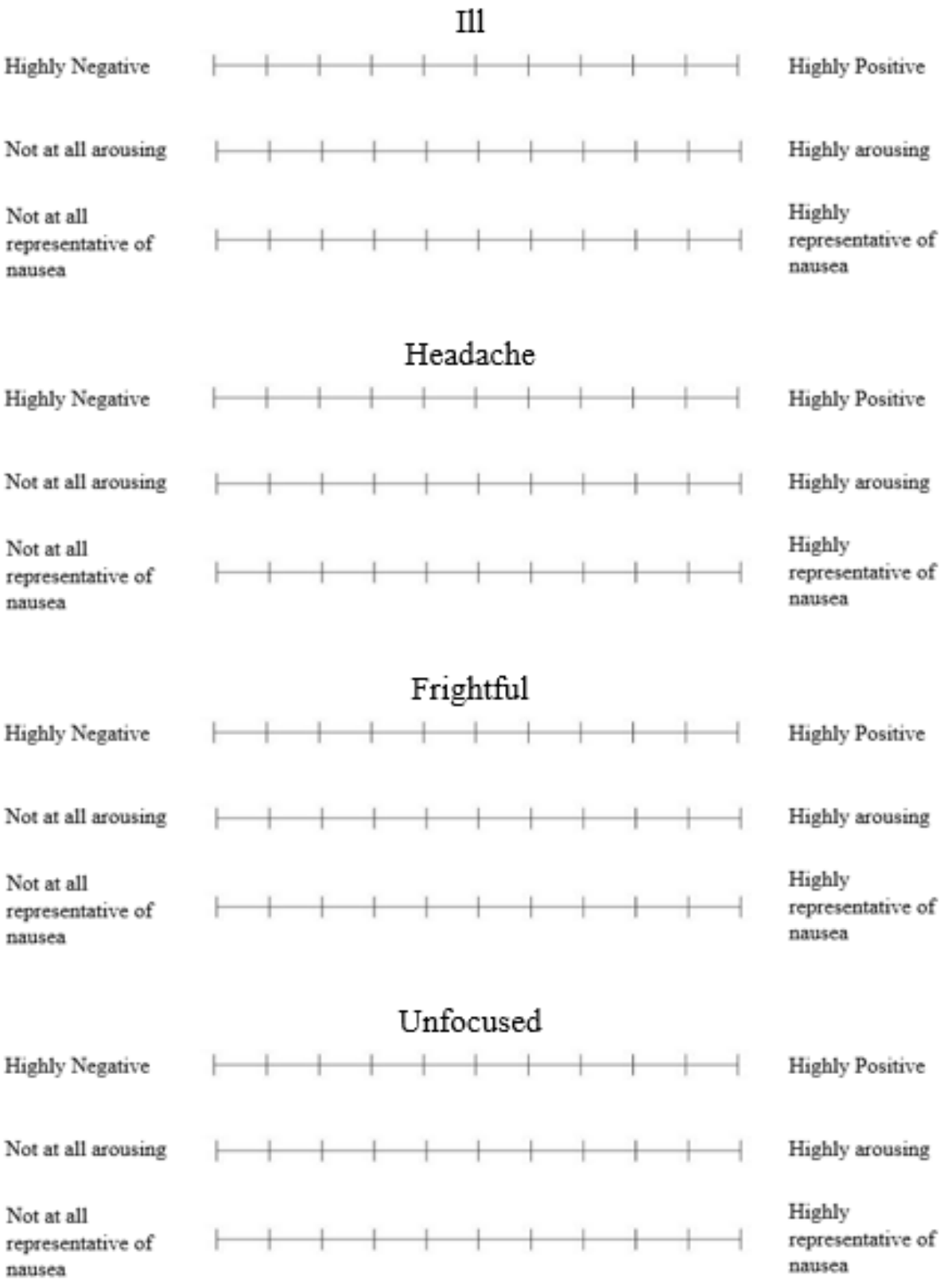
Hot

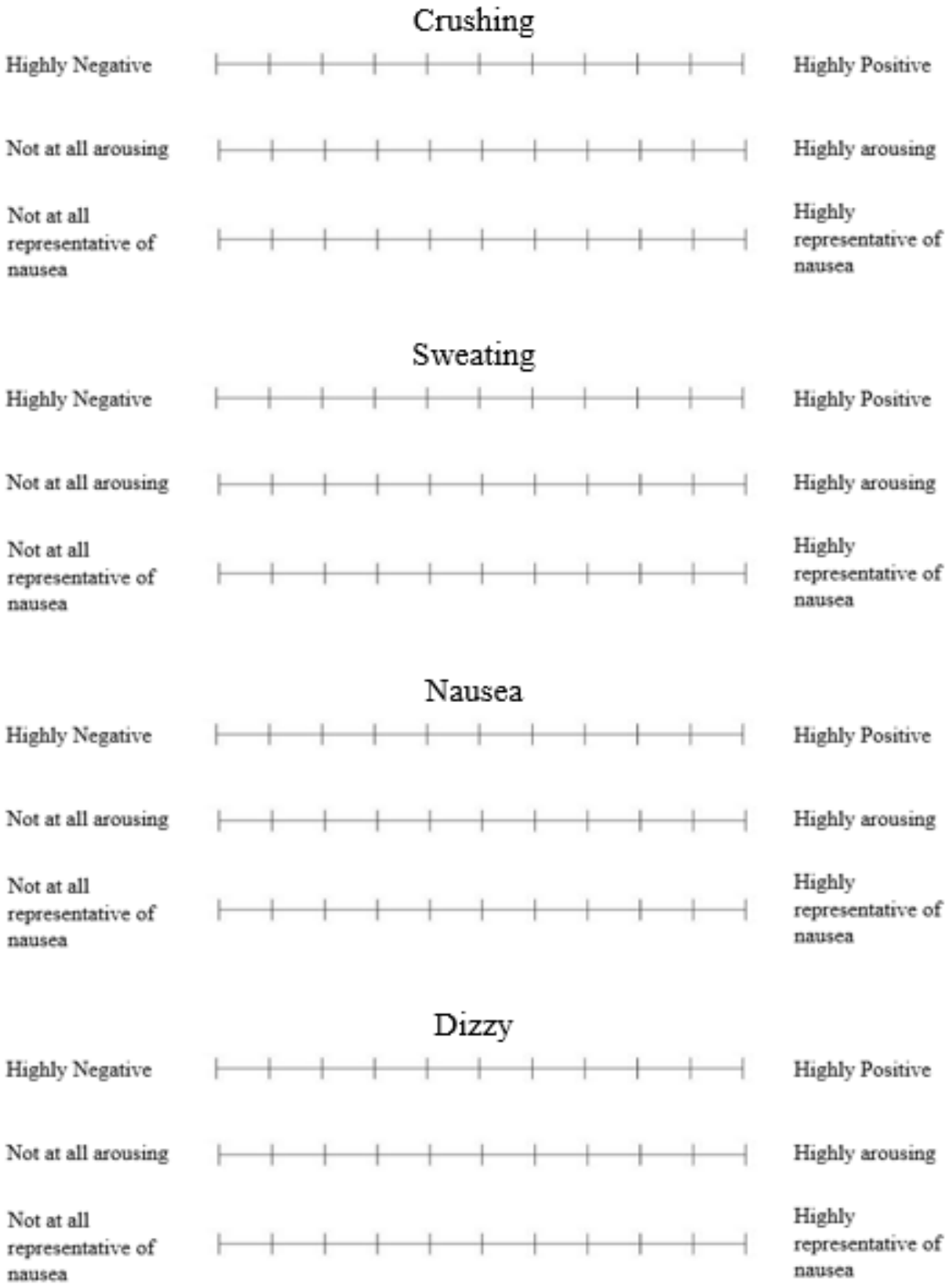
Highly Negative — Highly Positive

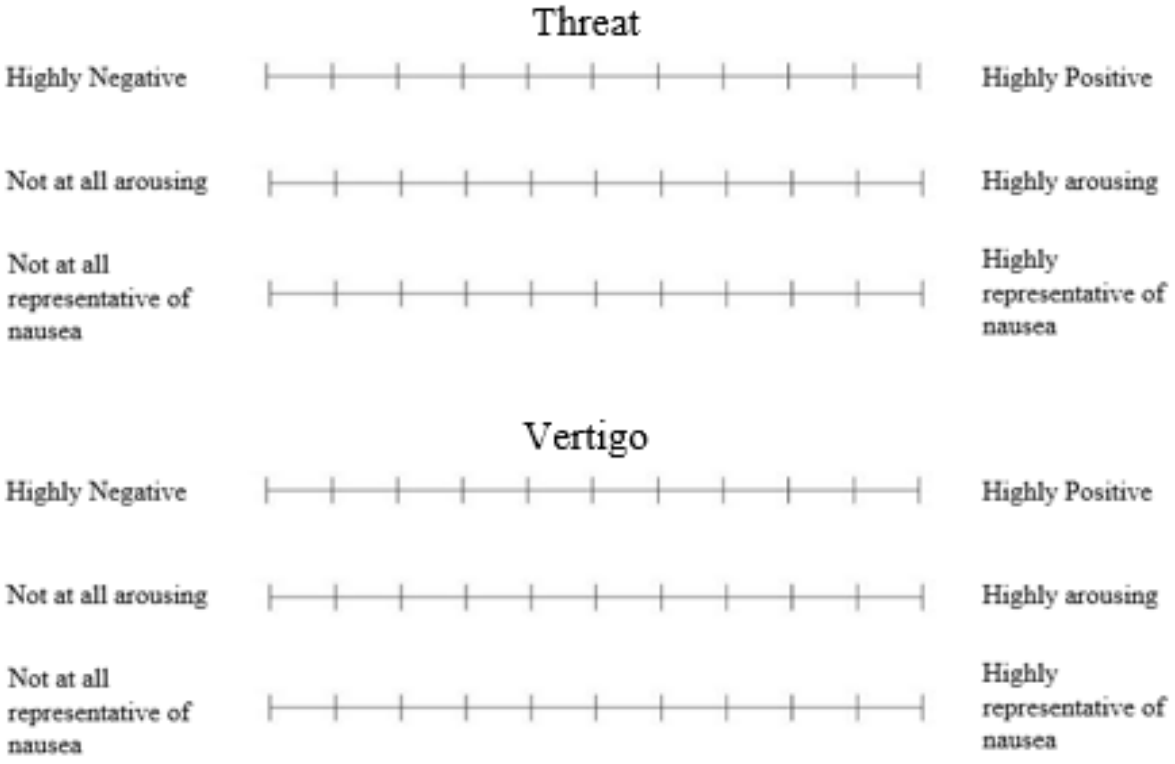
Not at all arousing — Highly arousing

Not at all representative of nausea — Highly representative of nausea


Warm
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Lightheaded
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Harmful
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Shaky
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea


Ill
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Headache
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Frightful
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Unfocused
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea


Crushing
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Sweating
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Nausea
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Dizzy
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea


Threat
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea
Vertigo
Highly Negative
Highly Positive
Not at all arousing
Highly arousing
Not at all representative of nausea
Highly representative of nausea

Selection of Nausea Stimuli for the Dot-Probe Task

Table H1

Pilot Ratings of Nausea and Threat Words for Nausea-relatedness, Arousal and Valence

Word	Word Type	Mean Nausea Rating	Mean Arousal Rating	Mean Valence Rating
Nausea*	Nausea	9.44	4.03	8.78
Vomit*	Nausea	9.41	4.97	9.28
Ill*	Nausea	7.77	3.40	8.37
Queasy*	Nausea	7.66	4.44	7.50
Sick*	Nausea	6.69	3.25	7.75
Vertigo*	Nausea	6.31	4.44	7.59
Dizzy*	Nausea	6.25	4.53	6.64
Lightheaded	Nausea	5.80	3.83	6.40
Headache*	Nausea	5.77	3.13	8.53
Shaky	Nausea	5.07	3.73	7.40
Sweating*	Nausea	4.81	4.63	6.03
Salivation	Nausea	4.50	4.63	5.63
Discomfort	Nausea	4.38	2.78	7.75
Hot	Nausea	3.19	5.31	4.06
Unfocused	Nausea	3.03	2.27	7.77
Weak	Nausea	2.88	3.06	7.72
Fatigue	Nausea	2.47	2.38	7.59
Eyestrain	Nausea	2.03	2.03	7.22
Exhausted	Nausea	1.94	2.59	7.47
Warm	Nausea	1.83	4.40	2.93
Harmful	Threat	3.20	4.00	9.07
Suffocating	Threat	2.97	5.03	8.63
Killing	Threat	2.50	4.94	9.25
Fearful	Threat	2.44	4.59	8.19
Danger	Threat	2.38	5.88	8.44
Terrifying	Threat	2.13	4.78	8.72
Crushing	Threat	2.09	3.19	7.53
Threat	Threat	1.84	4.63	8.56
Frightful	Threat	1.80	3.13	7.87
Scared	Threat	1.56	4.38	8.34

*denotes a word selected as a dot-probe stimulus

Top ten symptoms increased by VR exposure (Mao, 2018).

1. Nausea*
2. General discomfort*
3. Sweating*
4. Dizzy* (eyes open)
5. Dizzy* (eyes closed)
6. Stomach awareness
7. Vertigo*
8. Blurred vision
9. Fullness of head
10. Headache*

*denotes a word selected as a dot-probe stimulus

Words selected as nausea stimuli.

discomfort

dizzy

headache

ill

nausea

queasy

sick

sweating

vertigo

vomit

Matching Nausea Stimuli with Neutral Word Pairs

Table H2

Linguistic Characteristics of Nausea words selected for Dot-Probe Task.

Word	Length	Frequency ($log_{frequency}$ (HAL))	Number of syllables	Part of speech
discomfort	10	7.601	3	noun, verb
dizzy	5	7.553	2	adjective
headache	8	7.884	2	noun
ill	3	9.313	1	adjective, adverb, noun
nausea	6	7.249	2	noun
queasy	6	5.303	2	adjective
sick	4	10.004	1	adjective, noun, verb
sweating	8	6.941	2	verb
vertigo	7	7.639	3	noun
vomit	5	7.180	2	verb, noun

Table H3

Matching Criteria for Neutral Pair-Words for Dot-Probe Task

Characteristic	Matching Criteria
Length	exact
Frequency	exact
Number of syllables	±5% of $log_{frequency}$
Part of speech	matched on at least one, as many as possible if multiple

Final Stimuli for Dot-Probe Task

Table H4

Three Sets of Word Pairs used as Dot-Probe Stimuli in this Study.

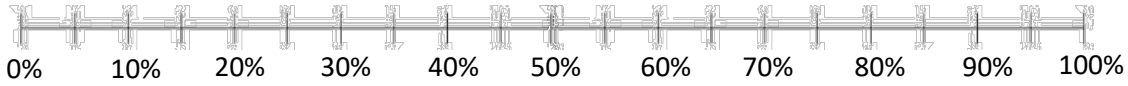
Nausea/Neutral (novel)	Threat/Neutral (Dehghani, Sharpe & Nicholas, 2003)	Neutral/Neutral (Keogh, Ellery, Hunt & Hannent, 2001)
Nausea/duplex	Crushing/elephant	Bleach/cooker
Vomit/opted	Fearful/tribune	Brushing/decorate
Ill/cod	Frightful/flowering	Container/staircase
Queasy/frilly	Terrifying/innovative	Furniture/magazines
Sick/bike	Killing/crystal	Housework/lightbulb
Discomfort/rebuilding	Suffocating/advertisers	Doorknob/bathroom
Sweating/commence	Scared/garage	Bedroom/surface
Dizzy/lyric	Danger/waited	Rack/plug
Headache/portrait	Harmful/airmail	Towels/bedspread
Vertigo/polygon	Threat/golden	Vase/tidy

Appendix I

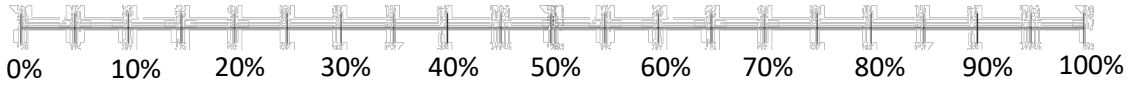
Expectancy and Anxiety Measures

How does motion affect our spatial ability in VR settings?

How likely do you expect it is that your balance will be affected in this VR session?



How likely do you expect it is that you will experience nausea in this VR session?



A number of statements which people have used to describe themselves are given below. Read each statement and circle the most appropriate number to the right of the statement to indicate how you feel right now, at this moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

	Not at all	Somewhat	Moderately	Very Much
1. I feel calm	1	2	3	4
2. I am tense	1	2	3	4
3. I feel upset	1	2	3	4
4. I am relaxed	1	2	3	4
5. I feel content	1	2	3	4
6. I am worried	1	2	3	4

Please make sure that you have answered *all* of the questions.

Appendix J

Transcript of VR Movement Instructions

Raise your left shoulder up and down three times.

Try to lift your left foot slightly off the ground.

Keeping your hands by your side, twist your torso as far to the left as you can.

Touch your nose with your left hand.

Try to lift your right foot slightly off the ground.

Keeping both feet flat on the ground, reach your right arm across the front of your body and twist your torso to the left.

Keeping your shoulders still, turn your head as far to the left as you can and then move it back to the centre.

Keeping your hands by your side, twist your torso as far to the right as you can.

Grasp both hands together in front of your body and then lift them up above your head and back down again.

Touch your nose with your right hand.

Reach both hands in to the air and look up towards the sky.

Bend slightly forwards at the waist while looking forwards.

Spend the next twenty seconds standing still and looking forwards.

Touch the back of your shoulder with your left hand.

Turn your head in a circular motion two times.

Draw a circle in front of your body with your left hand.

Stretch your right arm out to the side of your body and draw three circles in the air with your fingertips.

Raise your right shoulder up and down three times.

Put your left hand on your right shoulder and bend slightly forward.

Put your left hand on the top of your head and turn your torso to the left.

Touch your left shoulder with your right hand.

Spend the next ten seconds standing still and looking forwards.

Reach both hands out in front of you.

Place both hands on top of your head.

Clasp both hands above your head.

Look towards your right shoulder.

Touch your nose with both hands.

Touch the back of your shoulder with your right hand.

Pull your left shoulder and left ear towards each other.

Draw a circle in front of your body with your right hand.

participant is given the hand-held controller

Hold the controller out in front of you and press and hold at one o'clock for ten seconds.

Look up to the sky.

Tap the left side of the track-pad.

Tap the right side of the track-pad.

Move your finger from the bottom to the top.

Move your finger around the track-pad in a circular motion.

Swipe your finger across the track-pad from left to right five times.

Tap the centre of the track-pad.

Look down to the ground.

Hold the controller out in front of you and press and hold at nine o'clock for ten seconds.

Swipe your finger along the track-pad from top to bottom five times.

Move your finger around the track-pad once in an anti-clockwise direction.

You have ten seconds, try to move to the side.

Move your head in a circle two times.

Tap the top of the track-pad.

Hold the controller out in front of you and press and hold at three o'clock for ten seconds.

Turn your head towards the left.

With your thumb, quickly click the track-pad at two o'clock ten times.

You have ten seconds, try to move forward.

Move your finger around the track-pad once in a clockwise direction.

Turn your head towards the right.

Tap the bottom of the track-pad.

Hold the controller out in front of you and press and hold at one o'clock for ten seconds.

Appendix K

Manipulation Check

How does motion affect our spatial ability in VR settings?

What do you think was the purpose of this experiment?

Please turn over

Do you remember being warned about nausea as a possible side effect of VR?

☐ Yes

☐ No

How confident are you about this?

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

If yes, please fill in the information you were given about the likelihood of experiencing nausea as a side effect of VR.

___ out of 10 people will experience nausea at a level that bothers them

___ out of 10 people will **NOT** experience nausea at a level that bothers them

How much do you think your symptoms of nausea were caused by your use of VR?

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

How much do the following words relate to how you felt using VR?

Rebuilding

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

Vomit

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

Ill

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

Lyric	Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
	0	1	2	3	4	5	6	7	8	9	10
Frilly	Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
	0	1	2	3	4	5	6	7	8	9	10
Queasy	Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
	0	1	2	3	4	5	6	7	8	9	10
Opted	Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
	0	1	2	3	4	5	6	7	8	9	10
Sick	Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
	0	1	2	3	4	5	6	7	8	9	10
Duplex	Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
	0	1	2	3	4	5	6	7	8	9	10
Nausea	Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
	0	1	2	3	4	5	6	7	8	9	10
Discomfort	Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
	0	1	2	3	4	5	6	7	8	9	10
Cod	Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
	0	1	2	3	4	5	6	7	8	9	10

Bike

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

Sweating

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

Polygon

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

Dizzy

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

Headache

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

Portrait

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

Vertigo

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

Commence

Not at all		Slightly		Mildly		Moderately		Strongly		Extremely
0	1	2	3	4	5	6	7	8	9	10

Appendix L

Debrief Statement

How does motion affect our spatial ability in VR settings?

DEBRIEF STATEMENT

Details of the Study

Thank you for your participation in this research. The experiment was conducted by [redacted], under the supervision of [redacted]

Background

Nausea and vomiting are significant problems for many individuals undergoing simulated training in the aviation and aerospace sectors, as well as the military (Brooks et al., 2010; Webb, 2010-11). Recurrent symptoms of nausea ("cybersickness") occurring after Virtual Reality (VR) and simulator training have led some facilities to ground pilots for 6-12 hours subsequent to these sessions, reducing the individual's ability to work efficiently and potentially dissuading some from continued training (Lucertini, Mirante, Casagrande, Trivelloni, & Lugli, 2007). Nausea is also a significant problem in clinical settings, for example among those receiving chemotherapy treatment (Ben Colagiuri & Zachariae, 2010). This can result in an increased burden on healthcare resources and decreased quality of life for the patient (Bender et al., 2002). Identifying potential psychological mechanisms underlying the nauseous response that could ultimately lead to interventions to reduce nausea is therefore essential. In order to achieve such a goal, we first need to understand how factors such as our environment and expectations impact on nausea.

The present experiment investigates the role of negative expectancies on symptoms of nausea experienced as a result of VR. Specifically, an exacerbation of symptoms have been proposed to occur via the induction of negative expectancies (F. Benedetti, Lanotte, Lopiano, & Colloca, 2007; Ben Colagiuri, Quinn, & Colloca, 2015). Currently, VR technologies are sold with health warnings regarding potential side-effects that could arise from use, such as nausea, dizziness and disorientation. In the present experiment, we explore whether the wording and statistical information contained in such health warnings

can negatively impact on side-effects of VR-use. Understanding how instruction can induce nausea can be used to help combat unnecessary side-effects in the future.

In order to explore the role of instruction in the present expeirment, it was necessary to use a cover story to encourage you to believe that the primary outcome of the experiment was spatial awareness. This is because knowledge of the true aims of the experiment is likely to alter your performance. We apologise for this deception and hope that you will understand why it was required. We hope that the results of the experiment will ultimately lead to research that will help us find ways of reducing nausea.

The reason for delaying this information until now is so that other potential participants did not know that the study involved the role of expectancy before they participated. We apologise for this deception and for the delay in revealing the study's true aims. After reading this you have the right to withdraw your data from the study. Please inform one of the researchers if you wish to do this. Please be assured that there will be no repercussions if you choose to do this.

If you would like to know more about this study, please contact [redacted] or [redacted] or [redacted]

Meanwhile, because it is important that other participants do not know precisely what we are looking for before they are tested, we ask for your help by not telling other people that might participate in this study future.

The Role of Expectancy in the Present Experiment

In order to investigate the role of expectancy, we manipulated the VR software so that mild nausea should have been experienced (Yao et al., 2014).

Participants were randomly assigned to one of five conditions. 1) Positive framing of a likely side effect ("3 out of 10 people will not experience nausea"). 2) Negative framing of a likely side effect ("7 out of 10 people will experience nausea"). 3) Positive framing of an unlikely side effect ("7 out of 10 people will not experience nausea"). 4) Negative framing of an unlikely side effect ("3 out of 10 people will experience nausea"). 5) No framing (no additional warning is given following the consent process). The manipulation between positive and negative framing is known as an attribute framing effect, where positive framing of the same statistical outcome can lead to changes in behaviour [9]. In this study we also manipulated the statistical information contained in the warning – whether the risk of nausea was said to be likely (7/10) or unlikely (3/10). Based on past findings, we expected that

positive framing would reduce side effects relative to negative framing for 'unlikely' warnings [10-11] but that this effect would not be found for 'likely' warnings [12]. The no framing group acted as a control group to determine the effect of any additional warning regardless of framing or statistical information. Following the warning, your attentional biases were measured as they are hypothesised to play a causal role in producing framing effects.

Because VR-induced nausea has been suggested to arise due to sensory conflict between the vestibular, somatosensory and visual systems (Cevette et al., 2012; Cobb, Nichols, Ramsey, & Wilson, 1999; Davis, Nesbitt, & Nalivaiko, 2014), we also measured your postural instability using a Centre of Pressure Task (COP) on the Wii Balance Board (Chiarovano et al., 2015a). Different manipulations within the COP Task measure changes to the vestibular, somatosensory and visual system.

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Appendix M

Additional Statistical Output

Variable Names

Table M1

Descriptions of Variables in Additional Statistical Output

Variable Name	Description
Participant Attributes	
group	1 = control; 2 = negative frame, high-risk; 3 = negative frame, low-risk; 4 = positive frame, high-risk; 5 = positive frame, low-risk
Nausea Variables	
subscalepre	Score on SSQ nausea subscale at baseline
subscalepost	Score on SSQ nausea subscale at active measurement (following VR)
Postural Stability Variables	
A_Visual (SOT4/SOT1)	Active measure of visual contribution to postural stability (PS)
A_Vestibular (SOT5/SOT1)	Active measure of vestibular contribution to PS
A_Somatosensory (SOT2/SOT1)	Active measure of somatosensory contribution to PS
B_Visual (SOT4/SOT1)	Baseline measure of visual contribution to PS
B_Vestibular (SOT5/SOT1)	Baseline measure of vestibular contribution to PS
B_Somatosensory (SOT2/SOT1)	Baseline measure of somatosensory contribution to PS

congruence	Probe location relative to preceding target word (congruent = same position; incongruent = opposite position)
wordtype	Valence of word pair preceding probe (1: nausea; 2: threat; 3: neutral)
nauseacong	Mean response time of trials with nausea word pairs and congruent probes
threatcong	Mean response time of trials with threat word pairs and congruent probes
neutralcong	Mean response time of trials with neutral word pairs and congruent probes
nauseaincon	Mean response time of trials with nausea word pairs and incongruent probes
threatincon	Mean response time of trials with threat word pairs and incongruent probes
neutralincon	Mean response time of trials with neutral word pairs and incongruent probes
Manipulation Check Variables	
recallaccuracy	Accurate = matched absolute risk given in framed warning; inaccurate = did not match absolute risk given in framed warning

Postural Stability

Visual.

```
UNIANOVA A_VisualSOT4SOT1 BY group WITH B_VisualSOT4SOT1
  /METHOD=SSTYPE(3)
 /CONTRAST(group) = special(-1 .25 .25 .25 .25)
 /CONTRAST(group) = special(0 .5 .5 -.5 -.5)
 /CONTRAST(group) = special(0 .5 -.5 .5 -.5)
 /CONTRAST(group) = special(0 .5 -.5 -.5 .5)
  /INTERCEPT=INCLUDE
  /PRINT=ETASQ DESCRIPTIVE HOMOGENEITY
  /CRITERIA=ALPHA(.05)
  /DESIGN=B_VisualSOT4SOT1 group.
```

Tests of Between-Subjects Effects

Dependent Variable: A_Visual (SOT4/SOT1)

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	.003[a]	5	.001	.472	.796	.020
Intercept	.038	1	.038	30.117	.000	.203
B_VisualSOT4SOT1	.001	1	.001	.693	.407	.006
group	.002	4	.001	.419	.795	.014
Error	.150	118	.001			
Total	113.788	124				
Corrected Total	.153	123				

a. R Squared = .020 (Adjusted R Squared = -.022)

Custom Hypothesis Tests #1

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable A_Visual (SOT4/SOT1)
L1	Contrast Estimate		-.005
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		-.005
	Std. Error		.008
	Sig.		.544
	95% Confidence Interval for Difference	Lower Bound	-.020
		Upper Bound	.011

Test Results

Dependent Variable: A_Visual (SOT4/SOT1)

Source	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.000	1	.000	.369	.544	.003
Error	.150	118	.001			

Custom Hypothesis Tests #2

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable A_Visual (SOT4/SOT1)
L1	Contrast Estimate		-.003
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		-.003
	Std. Error		.007
	Sig.		.673
	95% Confidence Interval for Difference	Lower Bound	-.017
		Upper Bound	.011

Test Results

Dependent Variable: A_Visual (SOT4/SOT1)

Source	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.000	1	.000	.179	.673	.002
Error	.150	118	.001			

Custom Hypothesis Tests #3

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable A_Visual (SOT4/SOT1)
L1	Contrast Estimate		.000
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		.000
	Std. Error		.007
	Sig.		.970
	95% Confidence Interval for Difference	Lower Bound	-.014
		Upper Bound	.015

Test Results

Dependent Variable: A_Visual (SOT4/SOT1)

Source	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.000	1	.000	.001	.970	.000
Error	.150	118	.001			

Custom Hypothesis Tests #4

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable A_Visual (SOT4/SOT1)
L1	Contrast Estimate		-.008
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		-.008
	Std. Error		.007
	Sig.		.286
	95% Confidence Interval for Difference	Lower Bound	-.022
		Upper Bound	.007

Test Results

Dependent Variable: A_Visual (SOT4/SOT1)

Source	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.001	1	.001	1.148	.286	.010
Error	.150	118	.001			

```
REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA CHANGE
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT subscalepost
  /METHOD=ENTER subscalepre
  /METHOD=ENTER B_VisualSOT4SOT1
  /METHOD=ENTER A_VisualSOT4SOT1.
```

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics: R Square Change	F Change	df1	df2	Sig. F Change
1	.275[a]	.075	.068	12.177	.075	9.950	1	122	.002
2	.279[b]	.078	.062	12.211	.002	.306	1	121	.581
3	.300[c]	.090	.067	12.181	.012	1.594	1	120	.209

a. Predictors: (Constant), subscalepre

b. Predictors: (Constant), subscalepre, B_Visual (SOT4/SOT1)

c. Predictors: (Constant), subscalepre, B_Visual (SOT4/SOT1), A_Visual (SOT4/SOT1)

Vestibular.

```
UNIANOVA A_VestibularSOT5SOT1 BY group WITH B_VestibularSOT5SOT1
  /METHOD=SSTYPE(3)
 /CONTRAST(group) = special(-1 .25 .25 .25 .25)
 /CONTRAST(group) = special(0 .5 .5 -.5 -.5)
 /CONTRAST(group) = special(0 .5 -.5 .5 -.5)
 /CONTRAST(group) = special(0 .5 -.5 -.5 .5)
  /INTERCEPT=INCLUDE
  /PRINT=ETASQ DESCRIPTIVE HOMOGENEITY
  /CRITERIA=ALPHA(.05)
  /DESIGN=B_VestibularSOT5SOT1 group.
```

Tests of Between-Subjects Effects

Dependent Variable: A_Vestibular (SOT5/SOT1)

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	.003[a]	5	.001	1.008	.416	.041
Intercept	.020	1	.020	32.604	.000	.215
B_VestibularSOT5SOT1	.001	1	.001	2.353	.128	.019
group	.002	4	.000	.733	.571	.024
Error	.073	119	.001			
Total	124.389	125				
Corrected Total	.076	124				

a. R Squared = .041 (Adjusted R Squared = .000)

Custom Hypothesis Tests #1

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable A_Vestibular (SOT5/SOT1)
L1	Contrast Estimate		.006
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		.006
	Std. Error		.006
	Sig.		.288
	95% Confidence Interval for Difference	Lower Bound	-.005
		Upper Bound	.017

Test Results

Dependent Variable: A_Vestibular (SOT5/SOT1)

Source	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.001	1	.001	1.139	.288	.009
Error	.073	119	.001			

Custom Hypothesis Tests #2

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable A_Vestibular (SOT5/SOT1)
L1	Contrast Estimate		.002
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		.002
	Std. Error		.005
	Sig.		.621
	95% Confidence Interval for Difference	Lower Bound	-.007
		Upper Bound	.012

Test Results

Dependent Variable: A_Vestibular (SOT5/SOT1)

Source	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.000	1	.000	.246	.621	.002
Error	.073	119	.001			

Custom Hypothesis Tests #3

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable A_Vestibular (SOT5/SOT1)
L1	Contrast Estimate		.003
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		.003
	Std. Error		.005
	Sig.		.569
	95% Confidence Interval for Difference	Lower Bound	-.007
		Upper Bound	.013

Test Results

Dependent Variable: A_Vestibular (SOT5/SOT1)

Source	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.000	1	.000	.326	.569	.003
Error	.073	119	.001			

Custom Hypothesis Tests #4

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable A_Vestibular (SOT5/SOT1)
L1	Contrast Estimate		-.005
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		-.005
	Std. Error		.005
	Sig.		.275
	95% Confidence Interval for Difference	Lower Bound	-.015
		Upper Bound	.004

Test Results

Dependent Variable: A_Vestibular (SOT5/SOT1)

Source	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.001	1	.001	1.202	.275	.010
Error	.073	119	.001			

```
REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA CHANGE
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT subscalepost
  /METHOD=ENTER subscalepre
  /METHOD=ENTER B_VestibularSOT5SOT1
  /METHOD=ENTER A_VestibularSOT5SOT1.
```

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
					R Square Change	F Change	df1	df2	Sig. F Change
1	.287[a]	.082	.075	12.139	.082	11.055	1	123	.001
2	.302[b]	.091	.077	12.129	.009	1.210	1	122	.274
3	.304[c]	.092	.070	12.174	.001	.092	1	121	.763

a. Predictors: (Constant), subscalepre

b. Predictors: (Constant), subscalepre, B_Vestibular (SOT5/SOT1)

c. Predictors: (Constant), subscalepre, B_Vestibular (SOT5/SOT1), A_Vestibular (SOT5/SOT1)

Somatosensory.

```
UNIANOVA A_SomatosensorySOT2SOT1 BY group WITH B_SomatosensorySOT2SOT1
  /METHOD=SSTYPE(3)
 /CONTRAST(group) = special(-1 .25 .25 .25 .25)
 /CONTRAST(group) = special(0 .5 .5 -.5 -.5)
 /CONTRAST(group) = special(0 .5 -.5 .5 -.5)
 /CONTRAST(group) = special(0 .5 -.5 -.5 .5)
  /INTERCEPT=INCLUDE
  /PRINT=ETASQ DESCRIPTIVE HOMOGENEITY
  /CRITERIA=ALPHA(.05)
  /DESIGN=B_SomatosensorySOT2SOT1 group.
```

Tests of Between-Subjects Effects

Dependent Variable: A_Somatosensory (SOT2/SOT1)

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Corrected Model	.021[a]	5	.004	.952	.450	.039
Intercept	.040	1	.040	8.981	.003	.071
B_SomatosensorySOT2SOT1	.012	1	.012	2.566	.112	.021
group	.012	4	.003	.646	.631	.021
Error	.531	118	.004			
Total	107.817	124				
Corrected Total	.552	123				

a. R Squared = .039 (Adjusted R Squared = -.002)

Custom Hypothesis Tests #1

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable A_Somatosensory (SOT2/SOT1)
L1	Contrast Estimate		-.008
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		-.008
	Std. Error		.015
	Sig.		.585
	95% Confidence Interval for Difference	Lower Bound	-.038
		Upper Bound	.021

Test Results

Dependent Variable: A_Somatosensory (SOT2/SOT1)

Source	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.001	1	.001	.300	.585	.003
Error	.531	118	.004			

Custom Hypothesis Tests #2

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable A_Somatosensory (SOT2/SOT1)
L1	Contrast Estimate		-.006
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		-.006
	Std. Error		.014
	Sig.		.669
	95% Confidence Interval for Difference	Lower Bound	-.033
		Upper Bound	.021

Test Results

Dependent Variable: A_Somatosensory (SOT2/SOT1)

Source	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.001	1	.001	.184	.669	.002
Error	.531	118	.004			

Custom Hypothesis Tests #3

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable A_Somatosensory (SOT2/SOT1)
L1	Contrast Estimate		-.019
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		-.019
	Std. Error		.014
	Sig.		.171
	95% Confidence Interval for Difference	Lower Bound	-.046
		Upper Bound	.008

Test Results

Dependent Variable: A_Somatosensory (SOT2/SOT1)

Source	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.009	1	.009	1.897	.171	.016
Error	.531	118	.004			

Custom Hypothesis Tests #4

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable A_Somatosensory (SOT2/SOT1)
L1	Contrast Estimate		-.006
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		-.006
	Std. Error		.014
	Sig.		.638
	95% Confidence Interval for Difference	Lower Bound	-.033
		Upper Bound	.020

Test Results

Dependent Variable: A_Somatosensory (SOT2/SOT1)

Source	Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Contrast	.001	1	.001	.223	.638	.002
Error	.531	118	.004			

```
REGRESSION
  /MISSING LISTWISE
  /STATISTICS COEFF OUTS R ANOVA CHANGE
  /CRITERIA=PIN(.05) POUT(.10)
  /NOORIGIN
  /DEPENDENT subscalepost
  /METHOD=ENTER subscalepre
  /METHOD=ENTER B_SomatosensorySOT2SOT1
  /METHOD=ENTER A_SomatosensorySOT2SOT1
```

Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
					R Square Change	F Change	df1	df2	Sig. F Change
1	.275[a]	.075	.068	12.177	.075	9.950	1	122	.002
2	.275[b]	.075	.060	12.226	.000	.006	1	121	.939
3	.286[c]	.082	.059	12.237	.006	.799	1	120	.373

a. Predictors: (Constant), subscalepre

b. Predictors: (Constant), subscalepre, B_Somatosensory (SOT2/SOT1)

c. Predictors: (Constant), subscalepre, B_Somatosensory (SOT2/SOT1), A_Somatosensory (SOT2/SOT1)

Dot-Probe Data Sensitivity Analysis

```
GLM nauseacong threatcong neutralcong nauseaincon threatincon neutralincon
BY group
  /WSFACTOR=congruence 2 Polynomial wordtype 3 Polynomial
  /METHOD=SSTYPE(3)
  /SAVE=SRESID
  /PLOT=PROFILE(congruence*wordtype*group)
  /EMMEANS=TABLES(congruence) COMPARE ADJ(BONFERRONI)
  /PRINT=DESCRIPTIVE ETASQ HOMOGENEITY
  /CRITERIA=ALPHA(.05)
  /WSDESIGN=congruence wordtype congruence*wordtype
  /DESIGN=group.
```

Within-Subjects Factors

Measure: MEASURE_1

congruence	wordtype	Dependent Variable
1	1	nauseacong
	2	threatcong
	3	neutralcong
2	1	nauseaincon
	2	threatincon
	3	neutralincon

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
congruence	Sphericity Assumed	362.500	1	362.500	.867	.353	.007
	Greenhouse-Geisser	362.500	1.000	362.500	.867	.353	.007
	Huynh-Feldt	362.500	1.000	362.500	.867	.353	.007
	Lower-bound	362.500	1.000	362.500	.867	.353	.007
congruence * group	Sphericity Assumed	1747.516	4	436.879	1.045	.387	.032
	Greenhouse-Geisser	1747.516	4.000	436.879	1.045	.387	.032
	Huynh-Feldt	1747.516	4.000	436.879	1.045	.387	.032
	Lower-bound	1747.516	4.000	436.879	1.045	.387	.032
Error(congruence)	Sphericity Assumed	52237.407	125	417.899			
	Greenhouse-Geisser	52237.407	125.000	417.899			
	Huynh-Feldt	52237.407	125.000	417.899			
	Lower-bound	52237.407	125.000	417.899			
wordtype	Sphericity Assumed	995.644	2	497.822	1.003	.368	.008
	Greenhouse-Geisser	995.644	1.808	550.756	1.003	.362	.008
	Huynh-Feldt	995.644	1.891	526.394	1.003	.365	.008
	Lower-bound	995.644	1.000	995.644	1.003	.319	.008
wordtype * group	Sphericity Assumed	2800.989	8	350.124	.705	.687	.022

	Greenhouse-Geisser	2800.989	7.231	387.353	.705	.672	.022
	Huynh-Feldt	2800.989	7.566	370.219	.705	.679	.022
	Lower-bound	2800.989	4.000	700.247	.705	.590	.022
Error(wordtype)	Sphericity Assumed	124088.246	250	496.353			
	Greenhouse-Geisser	124088.246	225.972	549.131			
	Huynh-Feldt	124088.246	236.430	524.841			
	Lower-bound	124088.246	125.000	992.706			
congruence * wordtype	Sphericity Assumed	209.805	2	104.902	.177	.838	.001
	Greenhouse-Geisser	209.805	1.710	122.717	.177	.804	.001
	Huynh-Feldt	209.805	1.786	117.440	.177	.814	.001
	Lower-bound	209.805	1.000	209.805	.177	.675	.001
congruence * wordtype * group	Sphericity Assumed	1827.072	8	228.384	.385	.928	.012
	Greenhouse-Geisser	1827.072	6.839	267.167	.385	.907	.012
	Huynh-Feldt	1827.072	7.146	255.679	.385	.913	.012
	Lower-bound	1827.072	4.000	456.768	.385	.819	.012
Error(congruence*wordtype)	Sphericity Assumed	148285.695	250	593.143			
	Greenhouse-Geisser	148285.695	213.709	693.868			
	Huynh-Feldt	148285.695	223.311	664.031			
	Lower-bound	148285.695	125.000	1186.286			

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.	Partial Eta Squared
Intercept	155573531.800	1	155573531.800	3747.304	.000	.968
group	95450.646	4	23862.662	.575	.681	.018
Error	5189515.004	125	41516.120			

Nausea Analysis Excluding Inaccurate Recall

```
UNIANOVA subscalepost BY group WITH subscalepre
 /CONTRAST(group) = special(-1 .25 .25 .25 .25)
 /CONTRAST(group) = special(0 .5 .5 -.5 -.5)
 /CONTRAST(group) = special(0 .5 -.5 .5 -.5)
 /CONTRAST(group) = special(0 .5 -.5 -.5 .5)
  /METHOD=SSTYPE(3)
  /INTERCEPT=INCLUDE
  /CRITERIA=ALPHA(0.05)
  /DESIGN=subscalepre group.
```

Tests of Between-Subjects Effects

Dependent Variable: subscalepost

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	2680.148[a]	5	536.030	3.638	.004
Intercept	8810.211	1	8810.211	59.799	.000
subscalepre	1503.314	1	1503.314	10.204	.002
group	1403.700	4	350.925	2.382	.056
Error	16206.300	110	147.330		
Total	58292.000	116			
Corrected Total	18886.448	115			

a. R Squared = .142 (Adjusted R Squared = .103)

Custom Hypothesis Tests #1

Contrast Results (K Matrix)

group Special Contrast			Dependent Variable subscalepost
L1	Contrast Estimate		-5.762
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		-5.762
	Std. Error		2.643
	Sig.		.031
	95% Confidence Interval for Difference	Lower Bound	-11.000
		Upper Bound	-.523

Test Results

Dependent Variable: subscalepost

Source	Sum of Squares	df	Mean Square	F	Sig.
Contrast	700.041	1	700.041	4.752	.031
Error	16206.300	110	147.330		

Custom Hypothesis Tests #2

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable subscalepost
L1	Contrast Estimate		-4.611
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		-4.611
	Std. Error		2.667
	Sig.		.087
	95% Confidence Interval for Difference	Lower Bound	-9.896
		Upper Bound	.674

Test Results

Dependent Variable: subscalepost

Source	Sum of Squares	df	Mean Square	F	Sig.
Contrast	440.466	1	440.466	2.990	.087
Error	16206.300	110	147.330		

Custom Hypothesis Tests #3

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable subscalepost
L1	Contrast Estimate		1.968
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		1.968
	Std. Error		2.627
	Sig.		.455
	95% Confidence Interval for Difference	Lower Bound	-3.237
		Upper Bound	7.173

Test Results

Dependent Variable: subscalepost

Source	Sum of Squares	df	Mean Square	F	Sig.
Contrast	82.705	1	82.705	.561	.455
Error	16206.300	110	147.330		

Custom Hypothesis Tests #4

Contrast Results (K Matrix)

group	Special Contrast		Dependent Variable subscalepost
L1	Contrast Estimate		-2.060
	Hypothesized Value		0
	Difference (Estimate - Hypothesized)		-2.060
	Std. Error		2.632
	Sig.		.436
	95% Confidence Interval for Difference	Lower Bound	-7.276
		Upper Bound	3.157

Test Results

Dependent Variable: subscalepost

Source	Sum of Squares	df	Mean Square	F	Sig.
Contrast	90.191	1	90.191	.612	.436
Error	16206.300	110	147.330		

Appendix N

Variable Names for Raw Data File

Table N1

Descriptions of Variables Included in Raw Data File

Variable Name	Description
participant	Participant ID
group	Experimental group 1: control; 2: negative frame, high-risk; 3: negative frame, low-risk; 4: positive frame, high-risk; 5: positive frame, low-risk
frame	Frame of warning 0: negative; 1: positive
risk	Absolute risk of warning 0: low; 1: high
age	Age of participant (years)
gender	Gender of participant 1: female; 2: male
English	Participant's English experience 1: first language; 2: not first language but main language spoken at home; 3: neither first language nor main language spoken at home
VRexp	Participant's prior VR experience 1: some experience; 2: no experience
discomfort_base	Rating for current experience of 'general discomfort' at baseline 0-10
fatigue_base	Rating for current experience of 'fatigue' at baseline 0-10

headache_base	Rating for current experience of ‘headache’ at baseline 0-10
eyestrain_base	Rating for current experience of ‘eyestrain’ at baseline 0-10
focusing_base	Rating for current experience of ‘difficulty focusing’ at baseline 0-10
salivation_base	Rating for current experience of ‘increased salivation’ at baseline 0-10
sweating_base	Rating for current experience of ‘sweating’ at baseline 0-10
nausea_base	Rating for current experience of ‘nausea’ at baseline 0-10
concentrating_base	Rating for current experience of ‘difficulty concentrating’ at baseline 0-10
fullness_base	Rating for current experience of ‘fullness of head’ at baseline 0-10
blurred_base	Rating for current experience of ‘blurred vision’ at baseline 0-10
dizzyopen_base	Rating for current experience of ‘dizzy (eyes open)’ at baseline 0-10
dizzyclosed_base	Rating for current experience of ‘dizzy (eyes closed)’ at baseline 0-10
vertigo_base	Rating for current experience of ‘vertigo’ at baseline 0-10

stomach_base	Rating for current experience of ‘stomach awareness’ at baseline 0-10
burping_base	Rating for current experience of ‘burping’ at baseline 0-10
STAI_pre	Score on the STAI-6 at baseline. Summed item scores*20/6.
DASS_dep	Score on depression scale of DASS-21 at baseline. Sum of item scores*2.
DASS_anx	Score on anxiety scale of DASS-21 at baseline. Sum of item scores*2.
DASS_stress	Score on stress scale of DASS-21 at baseline. Sum of item scores*2.
DASS_total	Total score on DASS-21 at baseline. Sum of item scores*2.
expectancy	Response to “How likely do you expect it is that you will experience nausea in this VR session?” 0-100%
STAI_post	Score on the STAI-6 at active measurement. Summed item scores*20/6.
discomfort_active	Rating for current experience of ‘general discomfort’ at active measurement 0-10
fatigue_active	Rating for current experience of ‘fatigue’ at active measurement 0-10
headache_active	Rating for current experience of ‘headache’ at active measurement 0-10

eyestrain_active	Rating for current experience of ‘eyestrain’ at active measurement 0-10
focusing_active	Rating for current experience of ‘difficulty focusing’ at active measurement 0-10
salivation_active	Rating for current experience of ‘increased salivation’ at active measurement 0-10
sweating_active	Rating for current experience of ‘sweating’ at active measurement 0-10
nausea_active	Rating for current experience of ‘nausea’ at active measurement 0-10
concentrating_active	Rating for current experience of ‘difficulty concentrating’ at active measurement 0-10
fullness_active	Rating for current experience of ‘fullness of head’ at active measurement 0-10
blurred_active	Rating for current experience of ‘blurred vision’ at active measurement 0-10
dizzyopen_active	Rating for current experience of ‘dizzy (eyes open)’ at active measurement 0-10
dizzyclosed_active	Rating for current experience of ‘dizzy (eyes closed)’ at active measurement 0-10
vertigo_active	Rating for current experience of ‘vertigo’ at active measurement 0-10
stomach_active	Rating for current experience of ‘stomach awareness’ at active measurement 0-10

burping_active	Rating for current experience of ‘burping’ at active measurement 0-10
purpose	Response to “What do you think was the purpose of this experiment?” 1: matches cover story; 2: diverges from cover story but does not indicate knowledge of the true nature of the experiment; 3: indicates true knowledge of the experiment
recallaccuracy	Accuracy of recalled value given group membership 0: accurate for group; 1: inaccurate for group; 2: no statistic provided
rebuilding_rel	Response to “How much [does ‘rebuilding’] relate to how you felt using VR?” 0-10
vomit_rel	Response to “How much [does ‘vomit’] relate to how you felt using VR?” 0-10
ill_rel	Response to “How much [does ‘ill’] relate to how you felt using VR?” 0-10
lyric_rel	Response to “How much [does ‘lyric’] relate to how you felt using VR?” 0-10
frilly_rel	Response to “How much [does ‘frilly’] relate to how you felt using VR?” 0-10
queasy_rel	Response to “How much [does ‘queasy’] relate to how you felt using VR?” 0-10
opted_rel	Response to “How much [does ‘opted’] relate to how you felt using VR?” 0-10

sick_rel	Response to “How much [does ‘sick’] relate to how you felt using VR?” 0-10
duplex_rel	Response to “How much [does ‘duplex’] relate to how you felt using VR?” 0-10
nausea_rel	Response to “How much [does ‘nausea’] relate to how you felt using VR?” 0-10
discomfort_rel	Response to “How much [does ‘discomfort’] relate to how you felt using VR?” 0-10
cod_rel	Response to “How much [does ‘cod’] relate to how you felt using VR?” 0-10
bike_rel	Response to “How much [does ‘bike’] relate to how you felt using VR?” 0-10
sweating_rel	Response to “How much [does ‘sweating’] relate to how you felt using VR?” 0-10
polygon_rel	Response to “How much [does ‘polygon’] relate to how you felt using VR?” 0-10
dizzy_rel	Response to “How much [does ‘dizzy’] relate to how you felt using VR?” 0-10
headache_rel	Response to “How much [does ‘headache’] relate to how you felt using VR?” 0-10
portrait_rel	Response to “How much [does ‘portrait’] relate to how you felt using VR?” 0-10
vertigo_rel	Response to “How much [does ‘vertigo’] relate to how you felt using VR?” 0-10

commence_rel	Response to “How much [does ‘commence’] relate to how you felt using VR?” 0-10
target_rel	Sum of relatedness scores for target (nausea) words
neutral_rel	Sum of relatedness scores for neutral words
subscalepre	Score on nausea subscale of the SSQ at baseline. Summed: discomfort_base, salivation_base, sweating_base, nausea_base, concentrating_base, stomach_base & burping_base
subscalepost	Score on nausea subscale of the SSQ at active measurement. Summed: discomfort_active, salivation_active, sweating_active, nausea_active, concentrating_active, stomach_active & burping_active
nauseacong	Mean reaction time for dot-probe trials with nausea word pairs and congruent probes
threatcong	Mean reaction time for dot-probe trials with threat word pairs and congruent probes
neutralcong	Mean reaction time for dot-probe trials with neutral word pairs and congruent probes
nauseaincon	Mean reaction time for dot-probe trials with nausea word pairs and incongruent probes

threatincon	Mean reaction time for dot-probe trials with threat word pairs and incongruent probes
neutralincon	Mean reaction time for dot-probe trials with neutral word pairs and incongruent probes
percentcorrect	Percentage of correct dot-probe responses
nauseadiff	Difference in mean response times between incongruent and congruent trials for nausea word pairs nauseaincon – nauseacong
threatdiff	Difference in mean response times between incongruent and congruent trials for threat word pairs threatincon – threatcong
neutraldiff	Difference in mean response times between incongruent and congruent trials for neutral word pairs neutralincon – neutralcong
target_relavg	Mean rating on “How much do the following words relate to how you felt using VR?” (0-10) for target (nausea) words from the dot-probe task
neutral_relavg	Mean rating on “How much do the following words relate to how you felt using VR?” (0-10) for neutral words from the dot-probe task
nauseaavetime	mean response time for nausea trials on the dot-probe task (congruent & incongruent)

neutralavetime	mean response time for neutral trials on the dot-probe task (congruent & incongruent)
nauseadelay	difference in mean response time for nausea and neutral trials (nauseaavetime-nauseaavetime)
A_Visual (SOT4/SOT1)	Visual contribution to postural stability at active measurement A_EO_F (SOT4) ÷ A_EO_N (SOT1)
A_Vestibular (SOT5/SOT1)	Vestibular contribution to postural stability at active measurement A_EC_N (SOT5) ÷ A_EO_N (SOT1)
A_Somatosensory (SOT2/SOT1)	Somatosensory contribution to postural stability at active measurement A_EC_F (SOT2) ÷ A_EO_N (SOT1)
B_Visual (SOT4/SOT1)	Visual contribution to postural stability at baseline B_EO_F (SOT4) ÷ B_EO_N (SOT1)
B_Vestibular (SOT5/SOT1)	Vestibular contribution to postural stability at baseline B_EC_N (SOT5) ÷ B_EO_N (SOT1)
B_Somatosensory (SOT2/SOT1)	Somatosensory contribution to postural stability at baseline B_EC_F (SOT2) ÷ B_EO_N (SOT1)
DASS#_X	Responses to DASS-21 # = item number; X: D = item belongs to depression scale; A =

	item belongs to anxiety scale; S = item belongs to stress scale
calm_pre	Response to ‘calm’ item on STAI-6 at baseline
calmrev_pre	Reverse coded score for ‘calm’ item on STAI-6 at baseline
tense_pre	Response to ‘tense’ item on STAI-6 at baseline
upset_pre	Response to ‘upset’ item on STAI-6 at baseline
relaxed_pre	Response to ‘relaxed’ item on STAI-6 at baseline
relaxedrev_pre	Reverse coded score for ‘relaxed’ item on STAI-6 at baseline
content_pre	Response to ‘content’ item on STAI-6 at baseline
contentrev_pre	Reverse coded score for ‘content’ item on STAI-6 at baseline
worried_pre	Response to ‘worried’ item on STAI-6 at baseline
summed_pre	Sum of item scores for STAI-6 at baseline calmrev_pre + tense_pre + upset_pre + relaxedrev_pre + contentrev_pre + worried_pre

calm_post	Response to ‘calm’ item on STAI-6 at active measurement
calmrev_post	Reverse coded score for ‘calm’ item on STAI-6 at active measurement
tense_post	Response to ‘tense’ item on STAI-6 at active measurement
upset_post	Response to ‘upset’ item on STAI-6 at active measurement
relaxed_post	Response to ‘relaxed’ item on STAI-6 at active measurement
relaxedrev_post	Reverse coded score for ‘relaxed’ item on STAI-6 at active measurement
content_post	Response to ‘content’ item on STAI-6 at active measurement
contentrev_post	Reverse coded score for ‘content’ item on STAI-6 at active measurement
worried_post	Response to ‘worried’ item on STAI-6 at active measurement
summed_post	Sum of item scores for STAI-6 at active measurement calmrev_post + tense_post + upset_post + relaxedrev_post + contentrev_post + worried_post
withdrawal	Participant withdrawal status 0: did not withdraw, 2: withdrew

exclusion	Data exclusion for reasons other than withdrawal 0: data not excluded for a reason other than participant withdrawal; 1: data excluded for a reason other than participant withdrawal
A_EC_N (SOT5)	Postural stability with eyes closed and no mat at active measurement
A_EC_F (SOT2)	Postural stability with eyes closed and foam mat at active measurement
A_EO_N (SOT1)	Postural stability with eyes open and no mat at active measurement
A_EO_F (SOT4)	Postural stability with eyes open and foam mat at active measurement
B_EC_N (SOT5)	Postural stability with eyes closed and no mat at baseline
B_EC_F (SOT2)	Postural stability with eyes closed and foam mat at baseline
B_EO_N (SOT1)	Postural stability with eyes open and no mat at baseline
B_EO_F (SOT4)	Postural stability with eyes open and foam mat at baseline