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# User-centered digital interventions: tailoring relaxing places

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## List of Abbreviations

BFI: Big Five Personality Inventory

CBT: Cognitive Behavioral Therapy

EMDR: Eye Movement Desensitization and Reprocessing

eVR: engaging Virtual Reality

HCP: Hospitalized Cancer Patients

MAAS: Mindful Attention Awareness Scale

PTSD: Post Traumatic Stress Disorder

pVR: personalized Virtual Reality

PMR: Progressive Muscle Relaxation

RCT: Randomized Controlled Trial

rVR: relaxing Virtual Reality

SAM: Self-Assessment Manikin

STAI-Y: State-Trait Anxiety Inventory Form Y

VAS: Visual Analogue Scale

VE: Virtual Environment

VR: Virtual Reality

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## Abstract

Relaxation interventions can have psychological and physically beneficial effects.

In recent years, new technologies have begun to incorporate relaxation practices, to target stress and several psychological symptoms both in laypeople and patients suffering from psychological or medical conditions. However, in the field of digital interventions, it is still not clear which individual differences shape the preferences for specific relaxing contents or which features of the relaxation exercises can yield the best efficacy depending on the users. The present work aims to collect qualitative and quantitative data on users' preferences on relaxation experiences, to inform the creation of personalized digital relaxation intervention in the general population and cancer patients.

The six studies presented in the current project dealt with 1) the assessment of individual preferences on relaxation habits and autobiographical relaxing experiences in laypeople, 2) the evaluation of the features of the relaxing stimuli to be put inside digital interventions, which yield greater efficacy and are preferred by users (laypeople and cancer patients). Besides, a theoretical proposal for the incorporation of olfaction into digital interventions for personalized relaxation is provided.

Practical recommendations for the development of tailored relaxing interventions are derived considering the results of the included studies.

Specifically, personalized relaxation interventions should be built with the possibility of including body-focused techniques, with a variable degree of involvement required from users, as well as specific stimuli (i.e.: water, the sensation of warmth, avatars), and customizable perceptual features (i.e.: colours, sounds, scents).

# 1. Introduction

*1.1 Relaxation and meditation practice*

The relaxation response is a physiological and psychological state of deep rest, and it is the contrary of the stress or fight-or-flight response (Benson, Beary, & Carol, 1974; Dusek & Benson, 2009). The relaxation response can be reached when someone can be detached from habitual thoughts while concentrating on specific mental states or contents (a word, sound, prayer, sentence), or movements.

Mind-body techniques that induce relaxation comprise breathing exercises, several types of meditation practices, yoga, Tai Chi, Qi Gong, progressive muscle relaxation (Benson & Proctor, 2010). With the induction of a state of relaxation, some mind-body interventions can lessen chronic stress and enhance well-being (Cohen, Janicki-Deverts, & Miller, 2007). Evidence shows that relaxation response can be effective in treating the side effects of stress in persons struggling with anxiety (Nakao et al., 2001), insomnia (Jacobs et al., 1993; Morin, Gaulier, Barry, & Kowatch, 1992), and medical conditions or aging (Alexander, Langer, Newman, Chandler, & et al, 1989; Astin, Beckner, Soeken, Hochberg, & Berman, 2002; Galvin, Benson, Deckro, Fricchione, & Dusek, 2006; Hegde et al., 2011).

Notably, the relaxation response is paired with biochemical changes which are beneficial for the health. For example, the relaxation response is associated with modification in energy activity and resiliency of mitochondrial (Bhasin et al., 2013; Dusek et al., 2008), oxygen consumption (Chang et al., 2006), increased heart rate variability (Peng et al., 2004), and alterations in brain regions (Lazar et al., 2000).

Even though most of the mind-body techniques derive from millennia-old practices, over the last decades, new technologies have been increasingly applied to the treatment of psychological aspects (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014; Heber et al., 2017; Richards & Richardson, 2012), and had incorporated relaxation and meditation interventions (Mikolasek, Berg, Witt, & Barth, 2018; Toivonen, Zernicke, & Carlson, 2017).

Still, little is known on which exact features of these digital interventions are effective (the exercise, the modality used to deliver the intervention, etc) and on which individuals they are most effective. Furthermore, subjective preferences for relaxation are rarely assessed before the interventions and there is an overall lack of personalized interventions.

The present work deals with the personalization of digital relaxation experiences for both the general population and clinical samples. With 'relaxation experiences' here it is meant the subjective pleasant experience of being safe and calm, an experience that can be achieved with relaxation or meditation practices.

Relaxation is usually considered a behavioural approach that targets the development of a subjective psychophysiological response to counteract anxiety. Under the umbrella term of "relaxation techniques", as in the case of meditation, resides a variety of approaches, which can be carried out as single-session intervention or as prolonged training. Indeed, relaxation techniques include procedures ranging from muscle relaxation exercises (Bernstein & Borkovec, 1973; Jacobson, 1938), autogenic training (Schultz & Luthe, 1969), breathing control procedures directed to regulate the breathing frequency, muscles contractions, or both (such as square, abdominal or diaphragmatic breathing (Chen, Huang, Chien, & Cheng, 2017), cognitive or imaginary techniques derived from the Cognitive Behavioural Therapy (CBT), and a mixture of all these approaches.

Broadly speaking, relaxation is characterized by physiological reactions evoked by the absence of bodily and cognitive stresses and tensions and by the sense of being physically rested. Usually, those reactions are characterized by a lowering of neurological arousal together with a reduction in sympathetic activity (Esch, Fricchione, & Stefano, 2003). Physiological changes are also accompanied by the psychological advantage of the acquisition of a coping strategy that leads to the sense of control over symptoms of anxiety. Not unexpectedly, anxiety disorders and anxious states are frequently targeted with relaxation interventions, as relaxation exercises reduce the level of activation of the sympathetic nervous system (Taylor et al., 2003; Conrad & Roth, 2007; Chiang et al., 2009).

Indeed, as a recent meta-analysis showed, relaxation training yield to medium to large effect sizes in the treatment of anxiety (Manzoni, Pagnini, Castelnuovo, & Molinari, 2008).

In this meta-analysis also meditation practice, which interestingly resulted to be significantly effective in reducing anxiety symptoms, has been included in the 'relaxation training'. Not surprisingly, meditation is often considered a relaxation exercise, as meditation practice usually induces calm and serenity, which are the psychological sensations targeted by relaxation techniques. However, meditation does not derive from behavioural therapies and it is not primarily meant to be a relaxation exercise (Luberto, Hall, Park, Haramati, & Cotton, 2020).

Meditation is used during ancient contemplative and spiritual traditions and its classification is still wide-ranging and arbitrary. Interestingly, the brain patterns during meditations mostly differ across unique meditation traditions (Braboszcz, Rael Cahn, Levy, Fernandez, & Delorme, 2017).

Meditation(s) might be classified according to the spiritual tradition they are taken from (for example Transcendental Meditation, Zen, Sahaja Yoga, Vipassana) or according to the features of meditation activity. Depending on the technique, meditators are required to set a different weight on the focus of the mind activity during the practice. According to this last classification, recent cataloguing of meditation activities by Brandmeyer and colleagues (2019) identified up to six different types of practice.

Considering clinical efficacy, up to now the most well-known meditation interventions are Mindfulness-based interventions. As a simple definition, Mindfulness can be identified as being aware of one's experience in the present moment. It involves observing thoughts and emotions from moment to moment without judging or becoming caught up in them.

Mindfulness-based interventions, which have been initially developed by Jon Kabat-Zinn's in the Mindfulness-Based Stress Reduction model (Kabat-Zinn, 2003), have been widely employed throughout clinical settings, with a strong result for brain structure and activity,

immune responses, and endocrine markers (Jacobs et al., 2011, Pascoe et al., 2017, Schutte & Malouff, 2014), chronic pain, and sleep (Brandmeyer et al., 2019; Goldberg et al., 2018). Furthermore, considering mental health settings, Mindfulness-based interventions resulted to be effective for psychiatric conditions, even when compared to other evidence-based treatments (Goldberg et al., 2018; Katterman, Kleinman, Hood, Nackers, & Corsica, 2014). Overall, according to available evidence, both relaxation and meditation are valuable interventions for anxiety and stress-related conditions, with a small difference of efficacy between each other. A recent meta-analysis of 14 randomized controlled trials (N=862) compared the efficacy of relaxation and mindfulness approaches for anxiety (generalized anxiety disorder, social anxiety disorder, specific phobias, obsessive-compulsive disorder, or post-traumatic stress disorder; or high/stable anxiety). Results showed that meditation was slightly more effective in the treatment of anxious conditions even at 12-month follow-up (Goldberg et al., 2018).

Despite the evidence that those approaches are useful, little is known about which individual differences might shape relaxation experiences.

### *1.2 Individual differences and personalized approaches in relaxation*

Currently, there is little evidence about which psychological features and individual differences might shape the efficacy of relaxation and meditation practice among individuals. It is plausible to think that individual features and contextual factors, as in the case of hypnosis (Gruzelier, 2002), might shape the efficacy of those techniques.

To date, the main findings on the relationship between the individual features and meditation or relaxation regard gender differences and personality traits (i.e.: persistent patterns of behaviours, thinking, and emotions).

In a recent study from Conklin and colleagues (2018) on cellular longevity and meditation, authors found that meditation training can have a positive effect on telomere regulation and, even more interestingly for the present work, that this relationship was moderated by

individual differences in personality traits. Personality traits were measured with the widely used taxonomy of the Big Five Personality Traits (John, Naumann, Soto, 2008) and assessed with The Big Five Personality Inventory (BFI). The five traits are Openness (intellectual interest and artistic creativity); Conscientiousness (productivity and accountability); Extraversion (friendliness and confidence); Agreeableness (empathy and hope in others); Neuroticism (nervousness and tendency to develop anxiety and depression).

Specifically, the authors found that Agreeableness and Openness traits, moderated the efficacy of meditation training, enhancing telomers length. Neuroticism on the contrary moderated the relationship in direction of reducing telomers length and the degree of meditation activity.

In a sample of older adults, personality accounted for individual differences in the preference for the use of mindfulness techniques (Barkan et al., 2016). Specifically, personality traits are related to individual adoption of mindfulness techniques during and 6 months after the intervention, and they explained the amount of post-intervention mindfulness use, both directly and by promoting initial uptake of mindfulness during treatment. Specifically, the Openness trait was associated to choose a variety of techniques during and after the intervention, while agreeableness was related to greater use of meditation techniques during the intervention.

Considering gender differences, in a large survey conducted in the UK (Macinko & Upchurch, 2019), where 46 million people use to perform some type of meditation, two of the main factors that predicted meditation use were individual characteristics, including being female, and having health diseases (physical chronic diseases and pain, or anxiety/depression, and sleeping problems). Specifically, women and those who had health conditions were more likely to use meditation. In a survey with 34,342 participants conducted by Upchurch and colleagues (2019), authors found that both males and females perceived meditation to be effective and that a higher proportion of women used meditation

with yoga, Tai chi, or Qi gong, while men were tended to use specific types of stand-alone practices (e.g., mindfulness) than women.

Another study evaluated the association between personality traits, assessed with the BFI (John et al., 1991), and preferences for Autonomous Sensory Meridian Response (ASMR). ASMR is a perceptual condition in which audio-visual stimuli cause intense, pleasurable tingling sensations in the head and neck regions. It usually starts on the scalp and moves down the back of the neck and upper spine. Up to now, there are several online communities on ASMR (Fredborg, Clark, & Smith, 2017).

People who experienced stronger ASMR had significantly higher scores on Openness-to-Experience and Neuroticism, and significantly lower levels of Conscientiousness, Extraversion, and Agreeableness compared to matched controls (Fredborg, Clark, & Smith, 2017). Moreover, evaluations of subjective ASMR intensity in response to 14 common ASMR stimuli were positively correlated with Openness-to-Experience and Neuroticism. The authors concluded that results provided preliminary proof that ASMR is associated with specific personality traits.

Finally, considering gender influences on relaxation, a study by Kang and colleagues (2018) found specific patterns of use according to subjects' gender in a school-aged sample (female participants resulted to be more likely to use meditation), while Williams and colleagues (Williams, Van Ness, Dixon, & McCorkle, 2012) found that nor gender or age had an impact on the choice of meditating.

To date, the literature presents non-conclusive data on the influence that individual differences may have on meditation and relaxation preferences. Furthermore, except for personality traits, other psychological variables have been poorly explored.

*1.3 Digital relaxation and personalization*[1]

VR systems are a broad class of devices offering great flexibility and control and can be classified according to two main categories: immersive and non-immersive VR (Slater & Wilbur, 1997).

Non-immersive VR refers to devices such as computer screens, that connect users with a virtual world, but still allow for sensory communication with the external, real environment; immersive VR, on the other hand, offers a full immersion in the virtual world, providing a more realistic experience.

Specifically, "immersion" refers to the objective and measurable level of sensory fidelity a VR system can provide (Slater & Wilbur, 1997). When immersion is reached, physical reality is shut out, while the self-representation (i.e. a virtual body) within the virtual environment (VE) becomes more salient (Slater & Wilbur, 1997).

The subjective users' sensation of being there and state of consciousness (i.e. "presence") (Slater & Wilbur, 1997) consequently depends on the VR's level of immersion, provided by software and display technology (including all types of sensory displays) (Riva, Davide, & IJsselsteijn, 2003). As VR provides a safe environment within which different interventions can be carried on and as it can engage patients with multiple sensory modalities, it can ultimately offer various interventions ranging from trauma care, skin burns, to oncological care (Chirico et al., 2016b; Pourmand, Davis, Lee, Barber, & Sikka, 2017).

VR has also been successfully employed in the field of relaxation both in clinical and non-clinical settings.

To date, it is possible to recognize two main approaches to accomplish such aims across the literature.

The first one focuses on generic environments filled with relaxing narratives for the

[1] Adapted from Pizzoli, S. F. M., Mazzocco, K., Triberti, S., Monzani, D., Alcañiz Raya, M. L., & Pravettoni, G. (2019). User-centered virtual reality for promoting relaxation: an innovative approach. Frontiers in Psychology, 10, 479.

induction of control over one's own body and physiological response, while the second one engages the user in VR-mediated activities to empower his/her own abilities to regulate emotion (Pizzoli et al., 2019).

The first already used approach, which can be named "relaxing VR" (rVR henceforth), presents contents inspired or directly derived from classical relaxation techniques such as progressive muscle relaxation (PMR), autogenic training, yoga, meditation, and so on; typically, the user is shown environments that can help him/her feel safe and less tense.

Within the rVR approach, natural scenarios and visual or auditory natural elements have been frequently employed, showing a fair efficacy in several contexts (Annerstedt, Jönsson, Wallergård, Johansson, Karlson, Grahn, Hansen, Währborg, et al., 2013).

Often, VEs feature contents that are generically associated with pleasant, peaceful, non-arousing sceneries such as islands, parks, gardens, and other open-space, broad nature-based environments. Indeed, these environments proved to be a valuable mean to reduce stress conditions and promote relaxation (Baños et al., 2005; Felix, Ferreira, da Cruz, & Barbosa, 2017; León-Pizarro et al., 2007; Villani, Riva, & Riva, 2007), both in healthy and pathological contexts (e.g., pain) (Hoffman et al., 2011).

The second approach, which can be labeled "engaging VR" (eVR henceforth), requires a user's more active/interactive role and targets a learning process to empower users.

Under the umbrella term of 'eVR' can be classified as those interventions that try to build learning processes about one's own emotional and behavioral abilities, giving users a flexible and modifiable environment. This kind of approach does not merely imply a passive visualization of the VE or exposure to relaxing stimuli, rather it requires users to interact with virtual contents, allowing for the acquisition of specific skills. It is the case of emotion regulation training in VR and of some therapeutic interventions in VR. Indeed, VR therapy interventions have some overlapping characteristics with eVR, as the VEs vary according to the symptoms and the situation (pathology) to be addressed.

Therapeutically interventions with the VR have been employed for several

psychopathological conditions: anxiety disorders (Baños, Botella, Quero, García-Palacios, & Alcañiz, 2011; Gorini et al., 2010) specific phobias (Parsons, Rizzo, Rogers, & York, 2009), eating disorders (Ferrer-García & Gutiérrez-Maldonado, 2012; Ferrer-García, et al., 2013), trauma and stress-related disorders (Gonçalves, et al., 2012), as well as other serious psychiatric conditions (Maples-Keller, Bunnell, Kim, & Rothbaum, 2017).

Even if in these kinds of VR, a certain degree of content personalization exists, as VR addresses specific symptoms of the diseases, eVR is not systematically built on user-centered inquiries.

Overall, the rVR and eVR approaches make use of stimuli and environments, which have been chosen a priori and then tested on the users.

The scope of the present project is to extend the discourse on VR use to promote relaxation, by proposing a third tailored approach: a personalized relaxing VR (pVR).

This approach would be based on VR with personalized content, grounded on user research to identify important life events (Pizzoli et al., 2019).

The pVR would be a further step in the use of VR for relaxation, embracing and incorporating aspects of the two aforementioned approaches.

Specifically, this third approach would be different from the previous ones for what concerns the choice and the construction of VR contents and environments.

pVR would be a user- centered approach to the design and implementation of the VR setting itself, as user-centered approaches (e.g., based on users' feedback for content) have proved to be particularly effective in different applications of VR (Parsons & Reinebold, 2012; Rizzo & Shilling, 2018).

The design aspects regard the preliminary and specific investigation about users' relevant life events and preferences. Indeed, as the scenarios can have different effects depending on individual differences, it is important that the VE can display the users' preferred places (Kalevi M. Korpela, Ylén, Tyrväinen, & Silvennoinen, 2008; Kalevi Mikael Korpela & Ylén, 2009; Kyle, Graefe, Manning, & Bacon, 2004).

Some users may prefer warm, close, scarcely illuminated, and silent places, while others may suggest open spaces and illuminated scenes.

Besides, some users might benefit from specific categories of relaxing techniques, for example from cognitive and active narratives or passive and body-focused ones. Furthermore, considering the settings and the visual scenario, it has been shown that relaxation experiences linked to the natural landscape are shaped by individual differences (Song et al., 2013).

To evaluate and tailor interventions on users' preferences, the objectives of the present project are to gather users' autobiographical reports on past relaxing experiences, to assess users' preferences about relaxation strategies and tools as well as trying to profile users.

User-centered research could allow pVR to develop a trans-situational knowledge about the most common or recurrent multi-sensorial features of relaxing experiences, to develop a library of stimuli that can be used to approximate the personalized virtual scenario for each possible user.

To give a possible systematization for the collection of users' preferences, distinctive features of personal events might be rendered with symbols, activities, or other VEs contents, as showed in a preliminary diagram (See Figure 1).

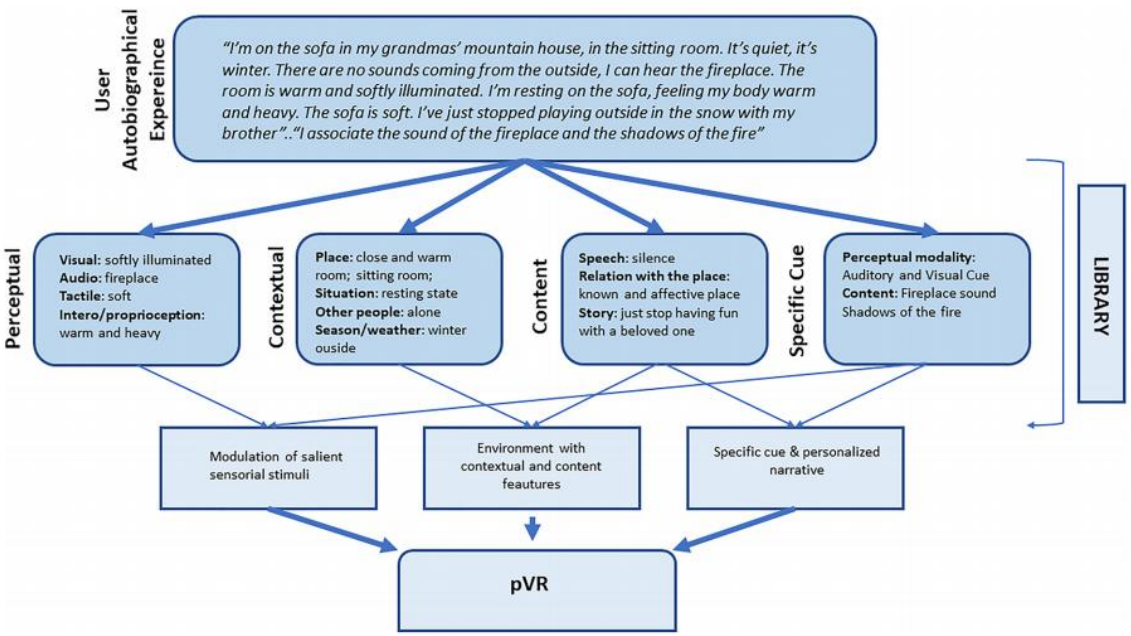


*Figure 1: pVR library flowchart.* The extraction process of relevant information to build pVR, to inform the construction of personalized environments. Adopting a pVR approach does not mean to digitally re-create specific situations, but to understand which symbols/features could be digitally rendered to allow the participants recall ancient sensations. From Pizzoli et al.; 2019

### *1.3.1 Tailor VR relaxing interventions for cancer patients*

#### *VR for cancer patients*

Relaxation for cancer patients proved to be an effective way to improve patients' mental state, pain, and the side effects related to the therapies (Charalambous et al., 2016; De Paolis et al., 2019; Kapogiannis, Tsoli, & Chrousos, 2018a; Zhang, Luo, & Zeng, 2017).

For instance, meditation and relaxation training can be used to target cognitive impairments linked to treatments (Zhang et al., 2017), while PMR, delivered with audio clips, has been proved to be effective in reducing anxiety and depressive symptoms (Holland et al., 1991). Furthermore, PMR combined with guided imagery can reduce pain (De Paolis et al., 2019), the impact of nausea and vomiting, and enhance patients' mental state (Kapogiannis, Tsoli, & Chrousos, 2018).

In recent years, the increased use of modern technologies and user-friendly tools in health care settings has allowed for novel treatments in clinical medicine. Among these devices, VR showed an emergent utility, not only because it makes it feasible to perform physicians'

skills training (for example with surgical training), but also because it gathered steam in being used for alternative or adjunctive patients treatments modalities (Dascal et al., 2017; de Rooij, van de Port, & Meijer, 2016; Dockx et al., 2016; Garrett et al., 2014; Hoffman et al., 2011; Indovina et al., 2018; Khor et al., 2016; Laver et al., 2017; Malloy & Milling, 2010; Maples-Keller, Yasinski, Manjin, & Rothbaum, 2017; Parsons et al., 2009; Penn, Rose, & Johnson, 2009; Rose, Nam, & Chen, 2018; Scheffler, Koranyi, Meissner, Strauß, & Rosendahl, 2017; Shin & Kim, 2015; Teo et al., 2016; M. Wang & Reid, 2011; Wiederhold, Riva, & Gutiérrez-Maldonado, 2016). Indeed, as promising results within the clinical application in different fields (pain management, physical rehabilitation, skills training, cognitive assessment, or cognitive therapy) became known, VR has been increasingly employed in health care settings (Pourmand et al., 2017).

For what concerns oncological settings, in particular, VR is a promising tool for supporting cancer patients and monitoring neuro-physiological and biological feedback during the intervention (Chirico et al., 2016).

Notably, people suffering from cancers are often a peculiar clinical target in the field of psychological treatment, as they display peculiar aspects, ranging from the discomfort of hospitalization (Mitchell et al., 2011), to suffering from painful and distressing procedures (Dorrepaal, Aaronson, & Van Dam, 1989), nausea and vomiting symptoms (Griffin et al., 1996; Kris et al., 1985) and psychological complaints about fear, sense of helplessness, fatigue (Pachman, Barton, Swetz, & Loprinzi, 2012; Theobald, 2004), anxiety and depression (Mitchell et al., 2011), and even post-traumatic stress symptoms (Arnaboldi, Riva, Crico, & Pravettoni, 2017).

From the first studies on the use of VR on cancer patients (Oyama, Ohsuga, Tatsuno, & Katsumata, 1999; Oyama, 1997), VR has been used to target different clinical outcomes and medical conditions within the field of cancer care (Chirico et al., 2016). However, the variety of VR interventions as well as the heterogeneity of patients and clinical variables targeted,

render an evidence-based evaluation of the applications of VR reality tools on cancer patients difficult.

Currently, the studies focused on this topic are 15 (Baños et al., 2013; Espinoza et al., 2012; Gershon, Zimand, Lemos, Rothbaum, & Hodges, 2003; Gershon, Zimand, Pickering, Rothbaum, & Hodges, 2004; House et al., 2016; Jahn, Lakowa, Landenberger, Vordermark, & Stoll, 2012; Kaneda, Oyama, & Katsumata, 1999; Li, Chung, & Ho, 2011; Marquess et al., 2017; Oyama et al., 1999; Oyama, Kaneda, Katsumata, Akechi, & Ohsuga, 2000; Schneider, Prince-Paul, JoAllen, Silverman, & Talaba, 2004; Tsuda et al., 2016; Vasterling, Jenkins, Tope, & Burish, 1993; Wolitzky, Fivush, Zimand, Hodges, & Rothbaum, 2005) and made use of miscellaneous mechanisms of actions to reach their aim, the most common one being a distraction.

In general, most of the studies have focused on anxiety and/or depression, aiming to improve participant's psychological conditions in those specific areas. Two studies use their VR method trying to induce positive emotions (Baños et al., 2013; Espinoza et al., 2012), while other interventions' focus is to alleviate negative emotions or negative moods, such as anxiety and depression. Other psychological variables considered are happiness, quality of life, hostility, and emotional status.

Almost all the studies consider a hospitalized sample and four are specific for a paediatric population (Gershon et al., 2003, 2004; Li et al., 2011; Wolitzky et al., 2005). In those, VR intervention is focused on reducing anxiety or depression through distraction, educative materials, and playing. Half of the studies conducted their interventions through an immersive VR instrument, with various technologies: some studies used head-mounted display or virtual glasses, while others use a complex system with for example a screen, a 3D sound system, foot devices, and a unit to deliver breeze.

When psychological constructs are evaluated, they are often associated with other variables, such as pain (often associated with anxiety), physical discomfort, fatigue, and neuropsychological measures. They are usually evaluated with validated self-report scales

(13/15) or rarely with instruments developed by the authors. Some studies consider also physiological measures, such as pulse rate, systolic and diastolic blood pressure, to demonstrate that physiological arousal has decreased after the VR intervention.

Overall, in the field of cancer care, VR intervention seems to have a positive effect on well-being and emotional dimensions.

*VR for relaxation in cancer patients*

To date, studies employing digital technology with the primary scope of relaxation in cancer patients are lacking, while there are studies aiming at improving psychological well-being, mood, and emotions, which can be considered quite similar to the relaxation state. Most studies that analyzed the effectiveness of VR for relaxation involved healthy participants and focused on experimental VEs and/or prototypes of products meant for healthy individuals. In some cases, VR for relaxation has been used specifically for patients with psychopathological conditions (for example General Anxiety Disorder, Specific Phobia, or PTSD) (Botella, Fernández-Álvarez, Guillén, García-Palacios, & Baños, 2017; Mishkind, Norr, Katz, & Reger, 2017; Park, Kim, Lee, Na, & Jeon, 2019). However, interest is growing towards using relaxing VR tools in healthcare and hospitalized contexts, such as cancer care. Cancer may lead to distressing and traumatic experiences, ranging from the communicational shock of the diagnosis, through treatment side-effects, active surveillance, and rumination about prognosis and the curse of the disease. Furthermore, cancer patients can display psychological issues such as depression (Massie, 2004; Rodin, 2014) fatigue and anxiety, (Tel, Tel, & Doan, 2011), and distress (Cook, Salmon, Hayes, Byrne, & Fisher, 2018; Meijer et al., 2013). For all these conditions, relaxation intervention might bring benefits for patients' well-being, as it helps address the physiological manifestations of prolonged stress (Scotland-Coogan & Davis, 2016).

Even if VR relaxing interventions might bring benefits to cancer patients, nowadays, design guidelines specifically dedicated to cancer patients are lacking.

Consequently, it is important to test innovative tools for promoting relaxation in patients, to evaluate not only tools' general functionality but also their adequacy to patients' experience and needs, as well as to identify the best practices for designing technologies suited for inclusion in disease treatment prescriptions (Triberti, Chirico, La Rocca & Riva, 2017; Triberti & Brivio, 2020).

## 1.4 Aim of the dissertation

The present project aims to better understand the individual features associated with relaxation preferences and to evaluate users' preferences on tools employed in relaxation (the type of exercises, the length, etc), to inform the construction of personalized digital relaxation interventions in the general population and cancer patients.

The present contribution contains works that employed both qualitative and quantitative methodologies, according to the specific aims of the studies.

Following the user-centered approach (Triberti, Chirico, La Rocca & Riva, 2017; Triberti & Brivio, 2020), the qualitative approach was preferred when the studies aimed to assess users' preferences, while the quantitative approach was used when the objectives of the studies were to compare the efficacy of relaxation experiences.

The studies that are presented in the next chapters dealt with a) understanding individual preferences for relaxing activities, b) comparing which features of digital relaxing stimuli might be more effective, and c) proposing the integration of olfaction into digital interventions for personalized relaxation. The chapters that report the empirical contribution of the present work have been divided according to the targeted sample (general population or cancer patients).

The first chapter of the empirical contribution, *Relaxation experiences for the general population*, deals with the personalization of relaxation experiences for people who do not suffer from specific medical conditions. The objectives of the included studies are to try to

explore the possible influence of individual differences on the preferences for relaxation habits, to evaluate personal autobiographical experiences with relaxation, and to test the efficacy of three relaxation exercises.

Specifically, the included studies aimed at:

1) testing a possible association between individual strategies in stress responses (coping style and trait anxiety) and relaxation preferences; classifying relaxation preferences according to common dimensions, to try to extract salient features to be used in future personalized interventions. The results might also provide additional evidence on the role of individual differences in the field of relaxation (*Relaxation preferences and individual differences in response to stressors*)

2) understanding which contextual and perceptual features of autobiographical relaxing experience people do remember the most since complex scenes or re-evoked perceptual elements might then be used to inform the construction of a library of digital stimuli (*The personal Safe Place*)

3) comparing the efficacy of different relaxation exercises and explore subjective experiences and preferences with the techniques. The assessment of the efficacy of remote exercise will provide evidence on which specific exercise might lead to greater efficacy when remotely delivered (*A comparison of remote relaxation experience: a randomized controlled study*).

The second chapter of the empirical contribution, *Relaxation interventions for cancer patients*, deals with the personalization of relaxation experiences for cancer patients. The objectives of the included studies were to evaluate the perceived need and the preferences for a digital relaxation intervention in hospitalized cancer patients, to assess the calming properties of a specific digital scenario, and to compare the efficacy of two exercises virtually delivered.

Specifically, the scopes of the studies were to:

1) assess hospitalized cancer patients' preferences and opinions on VEs for relaxations, during the hospitalization phase. The evaluation of such preferences and needs might then allow tailoring future relaxation interventions during the hospitalization period of cancer patients (*User-centered design on hospitalized cancer patients*)

2) test the relaxing properties of a specific VE. The assessment of the calming properties of the visual and auditive features of a specific scenario will provide a basis for the use of the scenario in future relaxation interventions (*The Waterfall environment*)

3) compare the efficacy of two guided relaxation techniques delivered with the VR and evaluate the preferences of breast cancer patients on the experience with the two techniques. These preliminary results might be a first step in the direction of the construction of a personalized intervention for non-hospitalized cancer patients (*Tailoring relaxing experience on breast cancer patients: a pilot study*).

Finally, the last chapter is a proposal for the employment of scents for relaxation, in VR interventions. The proposal focuses on the fact that current tools might allow for the inclusion of the sense of smell in the field of personalized relaxation. Given the emotional importance of the olfaction, this inclusion might enhance the efficacy of relaxation exercises (*The incorporation of olfactory cues in virtual environments for personalized relaxation*)

*Theoretical and clinical implications*

The following studies will provide empirical data on features that might inform the construction of personalized digital interventions for general relaxation and relaxation interventions in the field of cancer patients.

The data will regard the possible role of individual differences in relaxation preferences, the importance of some perceptual characteristics of the relaxing exercises, and the comparison of efficacy between different relaxation techniques digitally delivered.

Considering the spreading of eHealth technologies, which can provide effectively, yet fully automated interventions, it is important to deepen users' real needs and to plan the construction of interventions that can be tailored according to these needs.

The inclusion of preferences in digital interventions for relaxation might allow for the construction of user-centered digital prototypes, which in turn might lead to more effective and specific interventions.

# 2. Empirical contribution: Relaxation experiences for the general population

*2.1 Introduction to the research studies*

The following studies were conducted with mixed methodologies (quantitative and qualitative approaches) and they are meant to expand the knowledge on users' preferences on relaxation experiences.

In the next studies, three different elements were examined.

The participants of the studies were people which were asked for their relaxation preferences, for their autobiographical relaxation experiences, and for the perceived effectiveness of relaxing audio clips. These components were evaluated separately and with different methodologies, to collect data on the single features which might be used for the aim of personalization of future interventions.

Indeed, the aims of the studies were to 1) gather information about people's relaxation habits and the relationship between relaxation behaviours and individual traits, 2) examine relevant autobiographical relevant calm experiences, 3) test and compare the efficacy of guided exercises, provided with relaxing audio clips.

These data might inform the construction of future tailored digital relaxation interventions since they might shed light on the relationship between individual differences and relaxation preferences, and on the features of relaxing experiences that might lead to greater efficacy.

*2.2 Relaxation preferences and individual differences in response to stressors*

*Overview*

The study was focused on the relationship between the individual strategies used in stress responses (coping style and trait anxiety) and relaxation preferences.

The aims of the present study were to 1) assess if and to what extent individual differences might be associated with relaxation habits, 2) categorize relaxation preferences.

To reach this scope, an online survey assessing individual traits (trait anxiety and coping styles) and asking, with open-ended questions, relaxation habits among was used.

The study employed a mixed approach: a quantitative method was used to assess the association between individual traits, measured with questionnaires, and relaxation habits; a qualitative approach was employed for the evaluation of relaxation habits.

*Background*

At present, there are little data about which psychological features might influence the efficacy of relaxation practices among individuals.

It is realistic to assume that individual features and contextual factors, as in the case of hypnosis (Gruzelier, 2002), might shape the efficacy of relaxation techniques.

Currently, the only evidence on the impact of individual differences on the preferences for relaxation experiences in the general population focused on gender and personality traits (Barkan et al., 2016; Fredborg et al., 2017; Macinko & Upchurch, 2019). Specifically, personality traits of Openness and Agreeableness are associated with the use of a great variety of relaxation exercises and regular use of meditation, respectively (Barkan et al., 2016). Openness is also correlated with the choice of listening to ASMR (Fredborg et al., 2017), while gender is associated with the choice of using meditation, in particular female individuals, are more likely to use meditation (Macinko & Upchurch, 2019).

There is evidence on specific preferences on medical patients, such as stroke survivals (Wang, Smith, Ashley, & Hyland, 2019), people with chronic obstructive pulmonary disease (Hyland et al., 2016), and the caregivers of hematologic cancer patients (Vinci et al., 2018).

Hyland and colleagues (2016) for instance asked patients with the pulmonary disease to rate 6 different relaxation techniques according to the easiness of use and the likelihood to be used by themselves, finding out that in this type of patient, the instruction "Thinking of a nice place" is an effective and overlooked approach.

However, evidence on if and how individual differences can shape the preferences for relaxation habits still lack, while such results might help the construction of personalized interventions, built according to individual users' preferences.

Indeed, to date, data on the influence of individual differences on relaxing activity preferences are missing, while there is some evidence on the leisure activity preferences. Leisure activities are pleasant and recreation behaviours, that are not meant to be relaxing, and the individual tendency to choose the same activities seems to be stable over the years (Crawford, Godbey, & Crouter, 1986).

Considering leisure activities, Howard (1976) tried to investigate the relationship between selected variables of personality and leisure activity preferences, in a sample of high school students. The author used a structured questionnaire to assess the preferences for leisure activities and tried to assess the relationship between leisure activities and 14 personality needs (based on Murray's Need-Press Theory). The author concluded that the chosen variables of personality were significantly related to leisure activity preferences and that these results supported the view that different leisure activities appear to appeal to individuals with distinct needs and personality traits. The author extracted four independent leisure factors (outdoor-nature, sports, and aesthetic-sophisticate, and leisure detachment) and concluded that the use of selected variables of personality substantially increased the likelihood of correctly predicting leisure activity preferences.

Subsequent additional studies, on the general population, identified clusters of leisure activities based on the underlying psychological needs. Such clusters were used to build a taxonomy of leisure activities, with categories named agency, novelty, belongingness, service, sensual enjoyment, cognitive stimulation, self-expression, creativity, competition,

vicarious competition, relaxation, and a residual category (Tinsley & Eldredge, 1995; Tinsley & Johnson, 1984).

In the present study, firstly, specific patterns of relaxation preferences among participants' reports were analysed. Secondly, it was tested if individual characteristics on how persons react to stressors (trait anxiety and coping styles) were associated with relaxation habits among people belonging to the general population. To reach this purpose, an online survey with questionnaires and an open-ended question on relaxation habits were administered to people belonging to the general population.

To assess individuals' strategies and reactions in front of stressors, trait anxiety and coping strategies were assessed.

Trait anxiety indicates a quite durable trait related to individuals' personality (Spielberger 1979) and it reflects the tendency to react with anxiety under stressful circumstances. It can be thought of as a measure of the predisposition to experience emotional disorders and distress (Nordahl, Hjemdal, Hagen, Nordahl, & Wells, 2019).

Coping styles, on the other hand, represent behaviours that individuals enact in response to stressors.

It is possible to trace two classes of coping styles about the type of effort put in stressful situations: avoidant and approach coping (Carver, Scheier, & Weintraub, 1989b).

With avoidant coping, the person uses strategies to try to ignore or avoid the stressor and its emotional effects. This strategy is usually poorly effective at managing anxiety (Eisenberg, Shen, Schwarz, & Mallon, 2012). With approach coping, the person attempts to reduce or manage the stressors and their external or internal consequences (Aspinwall & Taylor, 1992; Endler & Parker, 1990; Suls & Fletcher, 1985; Tobin, Holroyd, Reynolds, & Wigal, 1989).

It is also possible to combine the avoidant and approach coping styles with two other independent coping categories: problem-focused coping and emotion-focused coping.

Problem-focused coping indicates the tendency to try to solve the problem, while emotion-focused coping means trying to reduce the emotional impact of the stressor (Folkman &

Lazarus, 1985; Lazarus & Folkman, 1984).

The combination of these four strategies leads to four coping types: approach problem-focused coping, approach emotion-focused problem, avoidant problem-focused coping, avoidant emotion-focused problem (Solberg Nes & Segerstrom, 2006).

In the present study, we hypothesized that persons' approaches and responses in front of stressors might shape the choice of relaxation habits.

Indeed, it has been shown that relaxation exercises (Eppley, Abrams, & Shear, 1989) or other activities such as physical exercise (Arcos-Carmona et al., 2011) have an impact on trait anxiety, in the direction of reducing trait anxiety scores, and that different levels of trait anxiety shape the personal experiences with meditation practices (Murata et al., 2004). However, it is still unclear if and to what extent trait anxiety is associated with the individuals' preferences for relaxation habits.

The same uncertainty concerns the influence of coping strategies on relaxation habits. To date, it is known that coping strategies resulted to be associated with individual strategies for the management of anxiety and panic attacks (Cox, Endler, Swinson, & Norton, 1992), and specific coping skills are required depending on the type of relaxation one wants to perform (Öst, 1987). Considering meditation and coping, two RCTs showed that mindfulness training produced less self-reported avoidance coping among relatively stressed individuals and that the mindful acceptance induction produced more approach and less avoidance coping than relaxation (Donald & Atkins, 2016).

### *2.2.1 Materials and method*

*Participants and procedure*

A convenience sample of 221 participants was recruited with a snowball method.

An invitation to take part in the study was published on Italian social media webpages (WhatsApp, Facebook). The readers were informed about the general aim of the study. Potential participants were encouraged to take part in the study and to share the invitation

with their acquaintances. The invitation contained a link to the Qualtrics platform, where a more detailed description was available. Overall, the survey lasted from 10 to 15 minutes.

The eligibility criteria to take part in the study were: 1) being older than 18 years old, 2) being a proficient Italian speaker, 3) having an appropriate familiarity with computer literacy. Before taking part in the study, participants were asked to read and complete an online consent form. The study was conducted according to the Declaration of Helsinki.

After completing the consent form, participants were presented with a sociodemographic questionnaire and then they were asked about relaxation preferences ("*What do you like to do to relax?"*; more than one answer was possible) and if they had experienced relaxation techniques such as autogenic training and so on.

Following these questions, participants were asked to fulfill the following questionnaire: 1) the State-Trait Anxiety Inventory (STAI-Y) (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) for the anxiety trait, with 20 items ("*I feel nervous*") on a Likert scale 1= rarely, 5=almost always; 6) the Brief COPE, the short version of the COPE scale (Carver, Scheier, & Weintraub, 1989a; Monzani et al., 2015), which assesses the four coping styles (approach problem-focused coping, approach emotion-focused problem coping, avoidant problem-focused coping, avoidant emotion-focused coping (Solberg Nes & Segerstrom, 2006)).

Descriptive statistics for the questionnaire are reported in Table 2. Overall, both the questionnaires showed a fair internal consistency; the mean score of STAI-Y was slightly higher than the mean of regulatory samples (Pedrabissi & Santinello, 1989).

Regarding participants, the sample comprises 79 (35.3%) female and 142 (63.8%) males; the mean age was 30 (*s.d.* =8.8) years (range: 18-71). Regarding educational levels, 6 (2.7%) have 8 years of educational level, 79 (35.7%) 13 years, 54 (24.4%) at least 16 years, 54 (24.4%) 18 years and 28 (12.7%) more than 20 years.

Considering occupational status, 156 (70.6%) are workers, while 65 (29.4%) retired, unemployed or students. For what concern marital status, 30 (13.6%) participants are

married, 3 (1.4%) divorced, 1 (0.5%) widow, 41 (18.6%) cohabitant, 70 (31.7%) in a stable relationship and 76 (34.4%) singles.

*Statistical Analysis*

Participants' relaxation preferences were classified according to 6 mutually exclusive categories, which were built based on distinctive features of the relaxation habits and considering the basic psychological needs, which drive pleasant activities, that were previously identified by Tinsley and Eldredge (1995). The categories were built by two researchers and were constructed starting from the taxonomy of Tinsley and Eldredge (1995). The two researchers independently identified hypothetical mutual exclusive categories after having read all the answers on relaxation habits. The common categories between the two researchers were kept, while the others were discussed.

The 6 categories were: 1) novelty and agency, 2) belongingness, 3) sensorial relaxation, 4) cognitive distraction, 5) creativity and self-expression, 6) substance use. Examples of each of the categories of relaxation habits and their absolute frequencies among all the reported relaxation habits are reported in Table 1.

The first category (novelty and agency) entails strategies based on the sense of control and of being able to perform specific actions, as well as on the need for being in contact with new and pleasant stimuli. The second category, belongingness, comprises relaxation habits that are focused on the feeling of closeness and affiliation with a relevant other. The third category, sensorial relaxation, deals with strategies that search for relaxation through body sensations and perceptions (temperature, textures, scents). The fourth category, cognitive distraction, refers to the need of shifting and devoting attention to external stimuli, while the fifth, creativity and self-expression, covers those strategies based on the need of expressing one's feelings artistically. The latter category, substance abuse, contains those behaviors that take advantage of the chemical effect of substances.

The influences of individual differences (coping strategies and trait anxiety) as well as psychosocial variables (age, gender) on relaxation habits were assessed through a

multinomial logistic regression with SPSS 26.0.

The first category was set at zero and used as a category of reference.

*2.2.2 Results*

Considering the experience with relaxation practices, 114 (51.6%) participants reported that they already tried at least one relaxation technique: mostly meditation and mindfulness (46), followed by yoga (30), Jacobsen, autogenic training, and Erikson technique (29) and respiration control (27). For what concern gender differences in having previous experience with relaxation exercises, female participants used relaxation practices more than male ($\chi^2(1)= 4.03$, p= .04), with a weak strength of association (Phi=.14, p<.05). Based on the odds ratio, the chance of having experienced relaxation techniques were 1.81 times higher for female than for male.

Considering relaxation habits, overall, the most reported strategies for relaxation dealt with sensorial relaxation, which included strategies such as hot showers, massages, laying on the bed and resting with eyes closed, and so on. The other preferred strategies were based on agency-novelty and cognitive distraction. Relaxation experiences with other relevant persons, based on self-expression and creativity, and substance abuse, were less reported.

The frequencies of each of the categories of relaxation habits among all the reported relaxation preferences are reported in Table 1. As regards the influence of individual differences in stress management strategies, the multinomial logistic regression (Table 4) shows the individual parameter estimates for each category compared to novelty-agency.

Regarding the category belongingness, results showed that having less avoidance problem-focused coping significantly predicted the possibility of using a relaxation strategy based on the need of belongingness, rather than on novelty-agency (b= -.06, Wald $\chi^2(1)= .03$, *p*= .03). The odds ratio showed that as avoidance problem-focused decreased by one unit, the change in the odds of using a strategy based on belongingness was .95. No other variables resulted to be significant in influencing the likelihood to use that strategy.

For what concern sensorial relaxation, results pointed out that having less approach problem-focused coping lead to an increase in the probability of using a strategy based on sensorial relaxation (change in odds of .59) rather than on novelty-agency (b= -.52, Wald $\chi^2(1)$= 2.9, *p*= .05). No other variables had a significant impact on that strategy.

As for cognitive distraction, the analysis showed that being male changed the odds of using a strategy based on cognitive distraction rather than on agency-novelty of 2.2 (b= .78, Wald $\chi^2(1)$ = 9.2, *p*= .002). No other significant results emerged from the analysis.

Considering self-expression and creativity, less approach problem-focused coping (b= -1.21, Wald $\chi^2(1)$= 6.19, *p*= .013) and being male (b= 1.73, Wald $\chi^2(1)$= 13.89, *p*= .0001) had a significant impact on whether participants chose a strategy based on self-expression and creativity, rather than on agency-novelty. Specifically, as approach-focused coping decreased by a unit, the change in odds of choosing relaxation based on self-expression and creativity was .3, while as gender changed from female to male, the change in odds was 5.6.

Finally, considering substance use, results showed that avoidance emotion-focused coping predicted the preference for a relaxation strategy based on substance use, rather than on novelty-agency (b= 1.05, Wald $\chi^2(1)$= .03, *p*= .03) and that when avoidance emotion-focused coping was one unit bigger, the change in odds ratio was 2.9. Being male rather than female also influenced the preference for relaxation strategies based on substance use (b= 2.5, Wald $\chi^2(1)$= 10.6, *p*= .001), with a change in the odds ratio of 11.9. No other variables resulted to be significant in influencing the likelihood to use that strategy.

Table 1 – *Classification of relaxation experiences*

| *Relaxation habits* | *Examples* | *Frequency (%)* |
|---|---|---|
| **Novelty and agency** | *Walking in new places*<br>*Play some sports* | 151 (21.6%) |

| | | |
|---|---|---|
| **Belongingness** | *Staying close to a beloved one*<br>*Meet with a friend* | 33 (4.7%) |
| **Sensorial relaxation** | *Having a hot bath*<br>*Massages* | 294 (42.1%) |
| **Cognitive distraction** | *Watching films*<br>*Reading books* | 145 (20.8%) |
| **Creativity and self-expression** | *Playing music or singing*<br>*Painting* | 45 (6.4%) |
| **Substance** | *Consuming alcohol*<br>*Using drugs* | 30 (4.3%) |

Table 2 – *Descriptive statistics of the questionnaires. Higher scores indicate a higher presence of the trait.*

| **Measure** | **Subscales Mean (*s.d.*)** | | | | **Cronbach alpha** |
|---|---|---|---|---|---|
| **STAI-Y** | *Trait Anxiety* | | | | |
| | 49.4 (11.2) | | | | .68 |
| **Brief COPE** | *Approach problem-focused coping* | *Approach emotion-focused problem* | *Avoidant problem-focused coping* | *Avoidant emotion-focused problem* | |
| | 2.9 (.6) | 2.6 (.5) | 1.9 (.7) | 2.1 (.6) | .75 |

Table 3*: Frequencies of relaxation strategies according to the gender of subjects*

| Gender | Novelty and agency | Belongingness | Sensorial relaxation | Cognitive distraction | Creativity and self-expression | Substance abuse |
|---|---|---|---|---|---|---|
| **Male** | 73 | 21 | 164 | 97 | 36 | 27 |
| **Female** | 76 | 11 | 129 | 48 | 8 | 3 |

Table 4*: Results of the multinomial logistic regression*

| | | **95% CI for Odds Ratio** | | |
|---|---|---|---|---|
| | *b (SE)* | *Lower* | *Odds Ratio* | *Upper* |
| | ***Belongingness*** | | | |
| Intercept | -1.54 | | | |
| Approach emotion-focused coping | .75 | .62 | 2.1 | 7.19 |
| Approach problem-focused coping | -.66 | .17 | .52 | 1.59 |
| Avoidant emotion-focused coping | -.38 | .29 | .68 | 1.59 |
| Avoidant problem-focused coping | -.06* | .47 | .95 | 1.89 |
| STAI-Y | .01 | .97 | 1.01 | 1.06 |
| Gender (male) | .65 | .81 | 1.91 | 4.49 |
| | ***Sensorial relaxation*** | | | |
| Intercept | 1.57 | | | |
| Approach emotion-focused coping | .34 | .75 | 1.40 | 2.62 |
| Approach problem-focused coping | -.52* | .33 | .59 | 1.07 |
| Avoidant emotion-focused coping | -.26 | .51 | .77 | 1.17 |
| Avoidant problem-focused coping | .12 | .79 | 1.13 | 1.61 |
| STAI-Y | -.01 | .98 | 1 | 1.02 |
| Gender (male) | .36 | .94 | 1.43 | 2.19 |

| | | | | |
|---|---|---|---|---|
| ***Cognitive distraction*** | | | | |
| Intercept | -.48 | | | |
| Approach emotion-focused coping | .38 | .70 | 1.46 | 3.03 |
| Approach problem-focused coping | -.35 | .36 | .71 | 1.40 |
| Avoidant emotion-focused coping | -.25 | .48 | .78 | 1.27 |
| Avoidant problem-focused coping | .07 | .71 | 1.08 | 1.63 |
| STAI-Y | .01 | .98 | 1.01 | 1.04 |
| Gender (male) | .78** | 1.32 | 2.2 | 3.63 |
| | | | | |
| ***Creativity and self-expression*** | | | | |
| Intercept | -.30 | | | |
| Approach emotion-focused coping | .91 | .81 | 2.48 | 7.55 |
| Approach problem-focused coping | -1.21** | .12 | .30 | .78 |
| Avoidant emotion-focused coping | -.41 | .32 | .66 | 1.39 |
| Avoidant problem-focused coping | -.30 | .41 | .74 | 1.34 |
| STAI-Y | .01 | .98 | 1.01 | 1.05 |
| Gender (male) | 1.73*** | 2.27 | 5.60 | 14.01 |
| | | | | |
| ***Substance use*** | | | | |
| Intercept | -3.25 | | | |
| Approach emotion-focused coping | .63 | .49 | 1.88 | 7.20 |
| Approach problem-focused coping | -1.08 | .11 | .34 | 1.07 |
| Avoidant emotion-focused coping | 1.05** | 1.40 | 2.90 | 5.89 |
| Avoidant problem-focused coping | .01 | .51 | 1.01 | 1.98 |
| STAI-Y | -.02 | .93 | .98 | 1.03 |
| Gender (male) | 2.5** | 2.68 | 11.90 | 53.24 |

$R2$ = .11 (Cox & Snell), .11 (Nagelkerke). Model $\chi2(30) = 70.32$, $p = .001$. * $p < .05$, ** $p < .01$, *** $p < .001$.

*2.2.3 Discussion*

Overall, most of the participants reported using relaxation strategies that involve sensorial relaxation. Having a bath with perfumed candles, listening to music while resting on the sofa, or other experiences which deal with body relaxation and sensorial stimulation were preferred the most. In all the sensorial relaxation strategies, participants have a rather passive role and are on their own. Instead, the second and the third most common strategies were based on novelty-agency and on cognitive distraction. The habits based on novelty-agency were quite active (walking, clean up the room), while those who relied on cognitive distraction took place with distracting or involving cognitive stimuli, such as films or books. Considering the variables which influence the chance of preferring a strategy compared to the novelty-agency one, the male gender emerged to enhance the probability of choosing strategies based on cognitive distraction, self-expression and creativity, and substance use. Even if they refer to the specific use of meditation practices, previous results on the influences of sex, concerning the choice of using mindfulness or not, have been reported in the literature (Kang et al., 2018). Thus, it is plausible to assume that gender might shape the preferences for at least some relaxation habits.

Gender did not explain the adoption of the strategies based on sensorial relaxation and belongingness, meaning that those behaviours were used with the same probability by males and females.

Furthermore, according to the results of the present study, trait anxiety, as assessed by STAI-Y, did not influence the preferences for specific strategies.

This result could be explained by the fact that trait anxiety, which indicates the constant predisposition to feel adverse emotions (such as fears, worries, and anxiety) across different settings, might influence other aspects of the relaxation habits. For instance, high or low trait anxiety might impact the frequency of behaviours focused on relaxation, rather than on the type of strategy. Furthermore, we could not rule out the possibility that the type of classification of the relaxation strategies had an impact on such results.

Significant results emerged for what regards coping styles.

Specifically, people with less approach problem-focused coping styles were more likely to use strategies based on sensorial relaxation, self-expression and creativity, and substance use, rather than on novelty and agency.

Thus, it seems that those who had a lower tendency of using strategies aimed at actively manage stressors are inclined to relax with strategies based on passive body relaxation (sensorial relaxation), the use of imagination and the expression of originality (self-expression and creativity), and the use of external substances with anxiolytic properties, such as alcohol or cannabis (substance use).

On the contrary, lower levels of avoidance problem-focused coping, which characterizes at least a momentary disentanglement and leaving of goal-related behaviours, were associated with a higher probability of using strategies based on the presence of other relevant people (belongingness), such as cuddles, spending time with a beloved one and so on.

Future studies might try to replicate these relationships and to assess a possible causal role of coping styles in the choice of relaxation habits.

*Limitations*

The present study suffers from some limitations. First, the definition of relaxation categories was quite arbitrary and based on a previous taxonomy of leisure activity (Tinsley & Eldredge, 1995; Tinsley & Johnson, 1984), which are only partially similar to relaxation strategies. Other classifications might be possible.

Second, subjects were asked about which relaxation habits they were used to make use of to relax. However, a specific definition of relaxation was not given. Consequently, it is possible that participants described activities that make them feel in different ways than calm and relaxed. Furthermore, the frequency of the preferred relaxation strategies was not asked. Thus, we could not assess the preference and priority of relaxation strategies within each subject. Furthermore, we could not assess if some relaxation habits are associated with specific stressors.

Reports were also heterogeneous and vague for what regards the details of the relaxation habits. Contextual features of the activities, the preference for one activity over the others, the time spent doing the activities, and their perceived efficacy were lacking.

*2.3: The personal Safe Place*

*Overview*

The use of autobiographical stimuli and personalization in the field of VR for psychological interventions is increasing (Heyse et al., 2019; Hu & Wang, 2010; Pizzoli et al., 2019). Available evidence points out that the use of autobiographical and personal contents might lead to a greater sense of presence and engagement inside the VR (Waltemate et al., 2018). However, autobiographical experiences are complex stimuli to be reproduced inside VEs. Autobiographical experiences might be put inside the VR in the form of autobiographical pictures, sounds clips, or virtual objects representing real items (toys, clothes, real landscapes). Furthermore, some virtual specific features associated with past real-life relaxing experiences might be reproduced in virtual scenarios (colours, sounds, etc).

Considering the possibility of reproducing such stimuli, for user-centered design, the present study aimed at gathering qualitative data on 1) autobiographical relaxing and calm experiences and 2) their unique perceptual and contextual features.

The study employed a qualitative approach since it is the more adequate method to examine narrative past experiences and to extract relevant perceptual and contextual features from the reports.

*Background*

To consider individual preferences and to give value to subjective experience, we conducted a qualitative study on autobiographic past calm and relaxing experiences.

The aim of the study was to gather information on the features of autobiographic safe and calm experiences, to try to extract specific features and/or stimuli, that will inform the construction of future personalized digital interventions. Such an approach was consistent with our hypothesis on the importance of conducting user-centered interviews on personal experiences, to build effective personalized digital interventions (Pizzoli et al., 2019)

To reach this objective, we interviewed healthy volunteers, asking them to describe a specific experience in which they felt calm and relaxed, while they were undertaking a relaxation

exercise. The reason why participants were interviewed during a relaxation practice was that we wanted to record the description of what subjects considered calm and relaxing, while they were in the target state of relaxation, and not when they only were thinking about a state of relaxation.

Participants were interviewed following a modified version of the technique 'Safe Place', also called 'Calm Place', from Shapiro (2001), combined with a breathing exercise.

Safe Place is one of the most frequent techniques derived from Eye Movement Desensitization and Reprocessing (EMDR) protocols, and it is utilized to induce a state of relaxation (Gerge, 2018). EMDR is a psychotherapy method originally employed to access and process traumatic memories (Shapiro, 2001). It is used to alleviate the suffering associated with disturbing past experiences.

The Safe Place technique is a component of the second stage of EMDR protocol, named "preparation", and in clinical settings, it can be useful when treating posttraumatic conditions (Cloitre, Garvert, Brewin, Bryant, & Maercker, 2013; Courtois & Ford, 2009) and severe dissociative disorders (Cardeña, Maldonado, Van der Hart, & Spiegel, 2009; Van der Hart, Nijenhuis, & Steele, 2006; Kluft, 1982, 1992a, b, 2009, 2012, 2013).

In the present study, Safe Place was chosen since it is an easy and effective technique to relax a person and to help to access memories.

For this study, a brief and simpler version of the technique was applied to healthy subjects.

### *2.3.1 Materials and Method*

#### *Participants and Procedure*

Participants were informed about the aim and the procedure of the study. Those who agreed to take part in the interview were interviewed following a modified version of the Francine Shapiro technique 'Safe Place', combined with breathing control instructions.

Overall, 20 volunteers took part in the study. Inclusion criteria were: 1) being Italian or Italian proficient speakers, 2) age between 18 and 70, 3) no psychiatric or neurological

diagnosis. Participants were told that they could stop the interview whenever they would like to, without the need of giving explanations for their choice. Before the interview, volunteers received detailed explanations on how the interview and the technique would have been conducted.

Volunteers were asked to re-evoke a safe autobiographical memory or an imaginary one if a real memory was too hard to remember. While re-evoking the memory, participants were guided into a relaxation state by an experimenter which was also a trained psychotherapist. The psychotherapist used breathing control instructions and gave alternate tapping on the hands of the participants (Shapiro, 2001). After the description of the safe place, participants were asked for a word they associated with the memory.

Compared to the standard technique by Shapiro (2001), which is applied following a more structured protocol, with dedicated questionnaires, we used only the bilateral sensorial stimulation and gave simpler instructions. The interviews lasted from 5 to 18 minutes.

Instructions were given as follows: 1. Participants were asked to take three deep breaths and think of a time when they felt completely safe, calm, and satisfied 2. Then they were required to remind the place or situation which generates feelings of calm and safety. They were also guided to focus their attention on the bodily sensations and the emotions related to the safe place; 3) The researcher then asked for a brief description of the scene and the associated sensations. The researcher also told the participants to take slow and deep breaths. 4) While the subjects were concentrated on the place, brief sets of bilateral hand stimulations were added (i.e.: brief and gentle alternate tapping on the hands); at the end of every brief set, participants were asked to describe further the place and their sensations. 5) Finally, participants were asked for a word or a sentence to associate with their place and a concluding brief set of stimulation closed the session.

After the end of the session, the researcher requested feedback on the experience and asked how the participants felt.

*Analysis*

Autobiographical experiences were audio-recorded and then systematized according to the features that were re-evoked by the subjects.

Three common dimensions of the reports were extracted and were used to classify the memories according to the type of the environment of the safe place (*setting*), the presence of other persons (*sharing*), and the type of activity that the subjects were doing in their safe places (*engagement*).

The sensorial experiences and the thoughts that were reported during the interviews were analysed too.

*2.3.2 Results*

All the participants reported feeling more relaxed and to be calmer after the interview. No subject reported distressing sensations.

Overall, 20 participants completed the study (male: 8, female: 12; mean age: 37, age range: 26-68). Among the 20 participants, 17 described a real memory, while three decided on an imaginary one. Six out of the 20 volunteers chose a memory from their infancy (between 7 and 11 age), while the remaining 14 chose an experience from adult life.

Persons who chose an imaginary safe place described natural landscapes (with wood, plants, lake, or sea) and imagined reading a book or resting while watching the panorama.

Personal autobiographical experiences were systematized according to the three dimensions *engagement*, *sharing*, and *setting*. The engagement was defined as the degree of personal engagement/activation in the safe place (on a continuum from physical activity to completely resting), sharing as the level of social and relation interaction (from intensively interacting to complete solitude), while setting was referred to the type of the environment (from close rooms to open natural landscape).

Considering the level of personal *engagement*, 15/20 re-evoked a memory in which they had a passive role (completely resting). Most subjects were resting, listening, or watching natural landscapes.

For what concern *sharing*, 13/20 reported an individual memory, where they were alone in a known or new place, 7/20 instead described the close presence of relevant others (close parents, partner, and friends). Regarding the *setting*, 15/20 reported open natural places natural (sea, forest, mountain, lake), while 5/20 described to be in a room (a homeroom, library room, and a bar).

Considering sensorial features, the dimensions that were described the most were hearing (natural sounds), the sense of warmth in the body, and the vivid colors (the sea, the wood). Except for three volunteers, all the participants reported memories that took place during the daytime; the remaining two spoke about memories at the sunset and the night.

The feeling of safety was linked mostly to bodily sensations (the body and/or the muscles calm or heavy) and to thoughts such as *"everything is ok"*, *"I am ok", "I am accepted as I am", "this is my place, I can be myself"*.

Some subjects (three) had difficulties in finding a safe memory or re-evoked also unpleasant feelings. Specifically, they initially found a memory that seemed to be calming and relaxing, but when they explored that memory, they remembered also triggers that made them remind unpleasant feelings and memories. A 33 years old female volunteer said *"Suddenly I feel sad.. I do not know why.. might be that part of the garden reminds me that my grandmother has gone away"*, while a 64 years old male subjects said that "*I never felt happier than in this moment, I which I could turn back time.. I realize how sad I feel now*".

*2.3.3 Discussion*

The entire sample reported feeling calm at the end of the session, even those who felt unpleasant emotions during the session. Notably, the original and complete technique is

effective in relaxing patients with trauma symptoms (Shapiro, 2001), thus we concluded that participants gave descriptions of the places while they were in a state of relaxation.

Overall, memories with natural settings and which took place during adult life were re-evoked the most. Furthermore, in many cases, subjects were not moving or resting in open spaces and they were alone or with one relevant person.

The sensorial features that were stressed the most during the reports were vivid colours, the sounds of waves or the wind, the warm sensations of the body, and the sense of resting and heavy muscles.

Almost all the memories took place during the daytime, even if some participants did prefer memories with lower illumination.

For future digital tailored interventions, a library of stimuli with the dimensions of engagement (from passive exercise to active ones), sharing (from solitude to some avatars), and setting (from a natural open spaced environment to close room) might be planned. Furthermore, it might be useful to provide the possibility of varying these dimensions on a continuum to allow subjects to personalize their interventions.

Additionally, according to the reports, it is likely that the possibility of personalizing and adding stimuli such as the sound of the wind, water (sea or lake), and mountains, three or grass, might increase the efficacy of relaxation exercises.

More importantly, considering the psychological experience and the thoughts that were associated with the places, the sense of acceptance seems to have a pivotal role in experiencing safety and relaxation.

Indeed, the safe places were memories where subjects felt that they were accepted, heard, or seen as they really were. Although these feelings cannot be reproduced visually with virtual stimuli, they might be reproduced through audio contents, for example, narratives, that might report sentences similar to the thoughts that participants had in their state of relaxation *"everything is ok"*, *"I am ok", "I am accepted as I am", "this is my place, I can be myself"*.

The same might be done to generate bodily sensations of warmth and heaviness of the muscles, for instance with narratives and techniques that guide the attention to bodily perception and muscle relaxation, such as progressive muscle relaxation or body scan.

Adding the features and personal preferences gathered from the users' preferred experiences might indeed provide more effective relaxation practices, delivered with personalized digital sessions.

Indeed, in the field of face-to-face exercises, an analogous technique was used in a study that compared the efficacy of six relaxation techniques in a sample of chronic obstructive pulmonary disease patients (Hyland et al., 2016). In that study, despite individual differences, most participants felt that the practice of "*thinking of a nice place*" was the most effective technique and the most probable to be practiced at home.

The authors concluded that familiarity is an important component for a relaxation technique to be easy and effective and that the ability to access the memory of previous relaxing and positive mood states might be helpful. Furthermore, these results were similar to those of a small study on the relaxation preferences amongst stroke patients, where there was a diffused preference for "thinking of a nice place" as a technique for relaxation (Wang et al., 2015). These results were also consistent with the findings that reported that adding positive content to relaxation techniques is helpful (Gaitan-Sierra & Hyland, 2014).

Finally, to produce experiences associated with past autobiographical memories, some caveats should be kept into consideration. Indeed, past autobiographical memories might be potent yet difficult stimuli to be managed, as shown by the participants that involuntarily associated painful memories and emotions with their safe places. Future studies should deepen the modality of examination of the autobiographical experiences, to further exclude the possibility of causing distress to users.

*Limitations*

The results should be judged considering some limitations. Firstly, as a taxonomy of relaxation experiences and of the features that characterize relaxing memories does not exist, results were analyzed according to categories that were built specifically for that study. Thus, other categories might be drawn and/or might be more informative.

Secondly, the efficacy of future digital tailored interventions featuring such personalized contents should be carefully tested in future studies. Indeed, at the current state, it is not possible to draw final conclusions on the efficacy of relevant features derived from autobiographical reports. The current study simply provides observational data on memories and on the possible features which might be used to improve the efficacy of future tailored interventions which employ digital technologies.

Third, the sample size of the study is limited. It is plausible that studies with larger samples might show different categories and/or features.

Lastly, we cannot rule out the possibility that the employment of other relaxation exercises, different from the safe place, might lead to different results or an enhanced state of relaxation in participants.

*2.4 A comparison of remote relaxation experience: a randomized controlled study*[2]

*Overview*

The present study aimed at comparing the efficacy of three different relaxation exercises. The study was built to examine and compare the distinct effect of three different relaxation techniques, digitally and remotely delivered.

The relaxation techniques employed in the study already proved to be effective in the field of relaxation, however, to try to find practices that can be used in remote personalized relaxation interventions, the techniques were modified to be suitable for digital and remote interventions.

The study employed a qualitative and a quantitative approach. The quantitative methodology allowed for an objective assessment of the efficacy of the exercises, while the qualitative one granted a user-centered evaluation of the particular experience of each participant.

The specific aims of the present randomized study were to 1) test whether remote relaxation practices like natural sounds, deep respiration, and body scan may promote relaxation and a positive emotional state and reduce psychomotor activation and preoccupation; 2) compare the efficacy between these techniques. Since the study was conducted during the COVID-19 pandemic and preoccupation was explicitly defined as preoccupations related to the COVID-19 pandemic; 3) evaluate the subjective experiences with the remote exercises.

*Background*

To limit the widespread of the virus SARS-CoV-2, from mid-March to May, Italy has faced a strict lockdown (World Health Organization., 2020). People were all in a suspended time, forced in a bubble with only a few family members or partner, otherwise alone. This condition of loneliness and social isolation had an impact on health and mental well-being, thus affecting vital functions (e.g., sleep quality), social relationships, and psychological

[2] Adapted from Pizzoli, S. M. F., Marzorati, C., Mazzoni, D., & Pravettoni, G. (2020). Web-Based Relaxation Intervention for Stress During Social Isolation: Randomized Controlled Trial. JMIR Mental Health, 2020;7(12):e22757.

status (Beutel et al., 2017; Courtin & Knapp, 2017; Leigh-Hunt et al., 2017). A recent review on the effects of the quarantine (Brooks et al., 2020) underlined that many people were facing several negative cognitive and emotional problems, like confusion, poor concentration, irritability, insomnia, distress, frustration, and anger. People were worried about the quarantine duration, insufficient information provision, economic problems, and shame. The associated negative affects impact the bio-psycho-social functioning and, in some cases, can lead to depressive or post-traumatic stress symptoms (Bai et al., 2004; Brooks et al., 2020).

The lack of a vaccine, the elevated chance of contagion, and the severity of symptoms - that sometimes leads to death – increased the risk perception. In high-risk situations, cognitive and rational thinking interacts with emotional appraisals, thus affecting the state of mind: individuals feel more vulnerable and may experience fear for themselves and their beloved ones (Renzi, Riva, Masiero, & Pravettoni, 2016; Slovic, Peters, Finucane, & MacGregor, 2005). Both physical and psychological dimensions are affected by the sense of uncertainty and the threat of contracting the virus. In this emergency condition, it is not uncommon for people to experience a psychophysiological hyperactivation, which is a state in which persons pay excessive attention to bodily sensations (Schmidt, Lerew, & Trakowski, 1997). Overall, COVID-19 and social isolation led to negative psychological effects, causing widespread concerns and psychophysiological reactions (Brooks et al., 2020).

Starting from these premises, it appeared of primary importance to develop efficacious interventions aimed at reducing the preoccupations about COVID-19 and the associated psychophysiological activation.

In this regard, previous studies demonstrated that interventions based on natural sounds, respiration, and meditation can help individuals to manage the effects of stress, by reducing physiologic arousal and restoring autonomic balance (Ditto, Eclache, & Goldman, 2006; Rainforth et al., 2007; Thoma, Mewes, & Nater, 2018; Wielgosz, Goldberg, Kral, Dunne, & Davidson, 2019). Listening to natural sounds significantly reduces human stress processes (Alvarsson, Wiens, & Nilsson, 2010; Ditto et al., 2006; Thoma et al., 2018), while guided

relaxation techniques represent widely used methods to produce a deep state of relaxation and enhance physical and emotional well-being. Deep breathing exercises and the focus of attention on body perception (body scan) are two of the main techniques to reduce hyperarousal and achieve a more relaxed condition. The first one may be also defined as “an efficient integrative body-mind training for dealing with stress, anxiety and psychosomatic conditions”(Ma et al., 2017); it may help to slow the breath, take in more oxygen, and reduce the use of shoulder, neck and upper chest muscles, thus achieving better emotional balance (Porges, 2001). The body scan instead aims at focusing attention on different parts of the body and becoming aware of the body's sensations, such as pain, tension, warmth, or relaxation (Gibson, 2019; Pizzoli et al., 2019). The application of these interventions on people who are forced into social isolation may contribute to the awareness of the mind-body condition and the reduction of negative effects.

We must add that, exactly because of the restrictions due to COVID-19, face-to-face interventions were not applicable, while internet-based interventions represented a good opportunity. The usefulness of remote interventions is also supported by studies that showed that online relaxation interventions yield psychological improvements, like in-person interventions (Jung et al., 2016; Kemper, Lynn, & Mahan, 2015).

To date, a comparison between remotely delivered natural sounds, respiration, and body scan meditation techniques is still missing in the literature.

The present study aimed at testing and comparing the efficacy of three remote interventions, respectively based on natural sounds, breathing regulation, and body scan, to find which intervention is the most effective for the target population. For this purpose, we tested the efficacy of three audio clips with the three relaxation practices (Square Breathing exercise, guided Body Scan exercise, and Natural Sounds) in stress reduction. Specifically, we expected to find: 1) a decrease in the levels of psychomotor activation/stress and of preoccupation for the COVID-19, as well as greater levels of relaxation and a better emotional state after the exposure of all the audio clips; 2) guided techniques (Square

Breathing and Body Scan) to have a superior effect on the above-mentioned dimensions, compared to Natural Sounds.

### *2.4.1 Materials and Method*

*Participants and Procedure*

During the first week of May 2020, the invitation to take part in the study was published on Italian social media webpages (specifically: WhatsApp, Facebook, Linked In, and Instagram). The readers were initially informed about the general aim of the study. Potential participants were encouraged both to take part in the study and to share the invitation with their acquaintances. The invitation contained a link to the Qualtrics platform, where a detailed description of the study was available.

The eligibility criteria were: 1) being older than 18 years old, 2) being a proficient Italian speaker, 3) not suffering from any impairment affecting auditive abilities, and 4) having an appropriate familiarity with computer literacy. Before taking part in the study, participants were asked to read and complete an online consent form.

The participation in the study consisted of three main parts: (a) a short questionnaire containing socio-demographics, the baseline anxiety evaluation (trait anxiety, anxiety for physical sensations, body vigilance) the pre-intervention evaluation, (b) the listening of a 7-minute audio-clip, (c) the post-intervention evaluation. The estimated time for participating in the study (completing the three parts) ranged from 12 to 17 minutes.

Participation in the study was voluntary and participants were informed that they could withdraw from the study whenever they wanted to. The research protocol followed the CONSORT-EHEALTH V1.6 Guidelines (Eysenbach & CONSORT-EHEALTH Group, 2011) and the Declaration of Helsinki (59th WMA General Assembly, Seoul, 2008). The research protocol was approved by the Ethical Committee of the University of Milan on April 30th, 2020, and registered with the International Registered Report Identifier (IRRID): PRR1-10.2196/19236 (Pizzoli, Marzorati, Mazzoni, & Pravettoni, 2020).

Overall, 294 completed at least the 75% of the survey. The sample was mainly composed by female participants (*F*=216, 73.5%, M= 78, 26.5%) and had a mean age of 39 years (*s.d.* 14.6, range: 18-78). Other descriptive statistics of the sample are reported in Table 5. The three groups were homogenous in sociodemographic variables like gender ($\chi^2(2) = .91$, $p$=.63), age ($F$ (2, 291) =1.59, $p$ = .21), educational level ($\chi^2$ (10) = 5.4, $p$=.86), marital status ($\chi^2$ (6) = 1.14, $p$=.98) and working condition ($\chi^2$ (6) = 3.5, $p$=.73).

*Baseline questionnaire*

After completing the sociodemographic form, participants were asked to report if they suffered from a chronic disease and how much the disease impacted their (perceived) vulnerability to COVID-19. Participants were also asked to answer questions on their job, the changes in their occupational status due to COVID-19 restrictions, and if they had prior experience with relaxation techniques.

Then, participants were asked to complete 3 self-assessed questionnaires aimed at measuring the current level of anxiety (trait anxiety), the tendency of being worried about physical signals and sensations (anxiety for physical sensations), and the degree of attention paid to bodily feelings (body vigilance). For the assessment of these characteristics, the following self-reported scales were used: the State-Trait Anxiety Inventory form-trait subscale (STAI-Y) ( Renzi, 1985; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983), the subscale physical concerns of the Anxiety Sensitivity Index-3 (ASI-3) (Petrocchi, Tenore, Couyoumdjian, & Gragnani, 2014; Taylor et al., 2007) and the Body Vigilance Scale (BVS) (Olatunji, Deacon, Abramowitz, & Valentiner, 2007).

The STAI-Y is a 20 items questionnaire, with a 4-point Likert scale from 1= ‘not at all’ to 4= ‘very much’) (Renzi, 1985; Spielberger et al., 1983), that assesses trait anxiety. The total score is the sum of all the items, after having computed the reverse scores of specific items. A higher total score indicates greater anxiety. The scale has a good internal consistency and it constitutes a reliable and valid tool for assessing anxiety symptoms in samples of healthy subjects (Potvin et al., 2011). In our sample, the Cronbach α was .84.

The subscale physical concerns of the ASI-3 is a 6 items subscale, that requires to rate on a 5-point Likert scale, from 0= ‘very little’ to 4 = ‘very much’, the strength of endorsement on how much worry is related to specific physical sensations. The total score is the sum of all the items (Pozza & Dèttore, 2015). In our study, the subscale physical concern had a high Cronbach α of .88.

Finally, the BVS is a questionnaire with 4 items on a scale from 0= ‘not at all like me’ to 10= ‘completely like me’, asking for how much attention one usually pays to body sensations. In the fourth item, participants had to rate their attention to 15 body sensations that are the core physical symptoms for panic attacks (Guze, 1995). In the present study, the internal consistency was .86.

*Manipulation*

After completing questionnaires, participants were randomly assigned to one of the three experimental groups via the randomization procedure of Qualtrics. The randomization option was set to enrol the same number of subjects in each condition.

In every experimental condition, participants received 7-minute audio aimed at promoting a state of awareness and relaxation. In the first experimental condition (i.e. Square Breathing), participants heard a recorded voice guiding the regulation of breathing frequencies to make every breathing act (inhalation, hold breath, exhalation, hold breath) lasting the same time (4 seconds). In the second experimental condition, audio with a voice that guided attention through every part of the body was presented. The voice gently requested the listener to feel tensions, unpleasant feelings and to let them go (i.e. Body Scan). Both tracks were recorded by a trained mindfulness and Yoga expert in collaboration with a psychotherapist and were pre-tested on 4 subjects to assess the easiness of the exercise and the perceived effectiveness. In the latter condition (i.e. Natural Sounds) participants were presented with a pre-recorded audio with natural sounds. All the audio clips were preceded by instructions on the place and the recommended body position for the exercises.

*Pre-post evaluation*

As pre-post measures (before and after the audio clips) subjects were asked to self-rate perceived relaxation level, perceived stress, and psychomotor activation, and how much they felt concerned about COVID-19. They were also asked to rate 3 specific features of their emotional state.

Specifically, participants were requested to evaluate, on a 3 Visual Analogue Scale (VAS) (0= not at all-10=completely), how much they felt relaxed, stressed/activated and how much thoughts related to COVID-19 scared them. Furthermore, participants completed the Self-Assessment Manikin (SAM) (Bradley & Lang, 1994) on emotional states. The SAM is a three-item visual scale (valence, intensity/arousal, dominance) commonly used to quantify the properties of the felt overall emotional state, on a 1 to 5 scale of images.

To check if participants really listened to the audio clips, they had to state, immediately after the audio clips, if they heard the entire trace, a part of it or no part.

Finally, all the participants were asked to describe their personal experiences and to provide suggestions for future changes. In particular, participants were requested to write a short paragraph answering two open-ended questions about their personal experience with the exercise (i.e. what they liked and what they would have changed).

*Statistical Analysis*

A detailed report of the data analysis approach can be found in the published protocol (Pizzoli et al., 2020).

To test the difference in efficacy between audio clips, a one-way ANOVA on the gain of relaxation levels, with 3 groups and fixed effects, with no interaction was performed, without considering subjects who stopped before the randomized exposure to the audio clips. Furthermore, to assess group and time effect and their interaction, a 2 (Time) x 3 (Groups) mixed-model ANOVA was performed on perceived relaxation scores, perceived stress/activation, and preoccupations related to COVID-19. We also did a nonparametric analysis on the items of SAM, as the statistical assumptions for parametrical analysis were

violated. In this case, we reported the effect size in the form of Hodges and Lehmann effect size.

Explorative analysis on the possible role of trait anxiety, anxiety for physical sensations, body vigilance in moderating the effect of the audio clips was also carried out. All the quantitative analyses were performed in SPSS version 26.0 (SPSS, Inc., Chicago, IL).

Qualitative answers on subjective experiences were organized into different categories, to systematize the suggestions and preferences. Participants' preferences on the remote relaxation interventions were organized into three different categories (audio features, relaxing feeling, and awareness). Finally, the suggestions for the improvement of the quality of the interventions were grouped into three main themes: audio features, clarity of instructions, and intervention's length.

### *2.4.2 Results*

*Sample description*

Overall, 328 participants were registered on the link of the survey. 294 gave written informed consent and completed more than the 75% of the survey (meaning that they complete the initial questionnaire and were randomized into the three conditions). 240 completed the entire survey and stated at the check that they listened to the audio clips: 77 in the Square Breathing group, 76 in the Body Scan group, and 87 in the Natural Sounds one.

Considering those who ended the entire survey (240), 70 (29.2%) had a chronic disease condition, while 170 (70.8%) had no chronic health issues. Fifteen (6.3%) reported being highly limited in daily activities because of a disease, while 26 (10.8%) were partially influenced by health issues and 97 (40.4%) were not affected in daily activities by health diseases. Descriptive statistics of the sample are reported in Table 5.

Considering the risk perception related to COVID-19, we found that participants felt a little danger of contracting COVID-19 (Mdn: 2= 'a little bit') and of having serious side effects for COVID-19 (Mdn: 2 = 'a little bit'). For what concern the degree of preoccupation for

different areas, participants reported to be moderately worried for their job, health, personal economic stability (Mdn: 3= ’quite a lot’), while they were more preoccupied with their own family (Mdn: 4= ‘a lot preoccupied’). Considering the previous experience with relaxation practices, 101 participants (42.1%) reported previous experiences with relaxation techniques, while 139 (57.9%) did not.

Table 5: *Descriptive statistics of the sample*

| *Sociodemographic Variables* | *Frequency (%)* |
|---|---|
| Educational Level<br>**N= 240** | |
| **Middle School diploma** | 12 (5.0) |
| **High school diploma** | 87 (36.3) |
| **Bachelor** | 33 (13.8) |
| **Master Degree** | 78 (32.5) |
| **Pos-Lauream** | 30 (12.5) |
| Marital status<br>**N= 240** | |
| **Single** | 68 (28.3) |
| **In a relationship** | 62 (25.8) |
| **Married or co-habitant** | 107 (44.6) |
| **Widower** | 3 (1.3) |
| Job Condition<br>**N= 240** | |
| **I have a job** | 184 (76.7) |
| **I do not have a job and I am not searching for it** | 42 (17.5) |
| **I do not have a job, but I am searching for it** | 14 (5.8) |
| Job Position<br>**N= 228** | |
| **Temporary job** | 38 (12.9) |
| **Permanent job** | 110 (37.4) |
| **Freelance** | 59 (20.1) |

| | |
|---|---|
| **Other types** | 21 (7.1) |
| Working activity in the last week<br>**N= 228** | |
| **Regular job activity** | 82 (27.9) |
| **Less than the regular job activity** | 50 (17) |
| **No activity** | 75 (25.5) |
| **Other** | 21 (7.1) |

*Trait anxiety, anxiety for physical sensations, and body vigilance*

Descriptive statistics and correlations between trait anxiety, anxiety for physical sensations, and body vigilance are provided in Table 6.

The three scores correlate moderately with each other, consistently with what has been found in previous literature (Olatunji et al., 2007; Pozza & Dèttore, 2015). Furthermore, there were small to moderate positive correlations between the post-exposure psychomotor activation/stress and preoccupation related to COVID-19. Finally, small negative correlations were found between trait anxiety and anxiety for physical sensations, and post-exposure perceived relaxation.

Table 6**:** *Descriptive statistics of the total scores of the questionnaire scores and correlations between total scores*

| *Questionnaire (N)* | *Mean (SD)* | *Median* | *Min-max* | *Correlation between total scores* | | |
|---|---|---|---|---|---|---|
| | | | | **STAI-Y** | **ASI-3** | **BVS** |
| STAI-Y | 44. 5 (8.2) | 43.5 | 28-68 | 1 | .422** | .343** |
| ASI-3 | 18.3 (7.9) | 18.5 | .3-39.7 | - | 1 | .517** |
| BVS | 11.4 (4.4) | 10.5 | 6-30 | - | - | 1 |
| | | | | ***Correlation with post-exposure measures*** | | |

| | | | |
|---|---|---|---|
| Relaxation | -.23** | -.13* | .1 |
| Psychomotor activation/stress | .48** | .38* | .3** |
| Fear related to COVID-19 | .19** | .35** | .21** |

** $p < .001$, $p < .05$*

For all three scales, higher scores indicated a higher presence of anxiety, and, overall, we found participants to have greater anxiety compared to regulatory samples.

Specifically, in man (M) and women (W) (M, Mean: 43.1, *s.d.*: 7.9; W, Mean: 45, *s.d.*: 8.3), the total score of the STAI-Y was slightly higher than the means reported for the regulatory samples (M, Mean: 36, *s.d.*: 9.7; W, Mean: 39.93 *s.d.*: 11) (Pedrabissi & Santinello, 1989).

Considering the ASI-3 subscale physical concerns (M, Mean: 10.1, *s.d.*:7.9; W, Mean: 18.7, *s.d.*: 7.8), we found participant to have higher levels of anxiety for physical sensations compared to the regulatory sample (M, Mean: 4.99, *s.d.*:4.28; W, Mean: 5.91, *s.d.*: 4.78) (Pozza & Dèttore, 2015). Finally, also for the BVS, (M, Mean: 17.4, *s.d.*:7.9; W, Mean: 18.7, *s.d.*: 7.8) participants reported higher body vigilance levels compared to the normative sample (M, Mean: 14.86, *s.d.*: 6.92; W, Mean: 15.95, *s.d.*: 9.71) (Olatunji et al., 2007).

The mean scores of the questionnaires were homogeneous between those who had a chronic disease and who had no health issues, except for the ASI-3 scores ($t(238) = -2.6$, $p = .01$). Specifically, persons with a chronic condition had significantly higher anxiety for physical sensations (Mean: 12.5; *s.d.:*5) compared to those who had no chronic diseases (Mean: 10.9; *s.d.:*3.9)

Furthermore, considering the total scores for each experimental group, we found that the three groups did not significantly differ in the initial scores of trait anxiety ($F$ (2, 237) =.02, $p = .98$), anxiety for physical sensations ($F$ (2, 237) =.09, $p = .92$) and body vigilance levels ($F$ (2, 237) =.17, $p = .85$).

*Perceived relaxation, psychomotor activation/stress, and thoughts related to COVID-19*

Descriptive statistics of all the assessed pre-post variables for each group are depicted in Table 7.

Table 7**:** *Descriptive statistics of all the assessed pre-post variable for each group*

| *Variables* | *Mean ± s.d.* | | | | | |
|---|---|---|---|---|---|---|
| | ***Square Breathing*** N= 77 | | ***Body Scan*** N= 76 | | ***Natural sounds*** N= 87 | |
| | Pre | Post | Pre | Post | Pre | Post |
| Relax | 47.7 ± 23.7 | 65.9 ± 20.4 | 47.4 ± 23.1 | 64.8 ± 23.9 | 44.7 ± 25.6 | 60 ± 23.8 |
| Psychomotor activation/stress | 48.5 ± 25.3 | 31 ± 22.7 | 49.8 ± 26.2 | 31.4 ± 22.7 | 57.4 ± 25.5 | 38.9 ± 26.9 |
| Fear related to COVID-19 | 62.6 ± 26.6 | 47.5 ± 27.8 | 64.6 ± 26.9 | 51.4 ± 28 | 66.6 ± 25.3 | 54.3 ± 27 |
| | *Median ± IQR* | | | | | |
| Valence | 5 ± 2 | 7 ± 2 | 5 ± 4 | 7 ± 3 | 5 ± 4 | 6 ± 3 |
| Arousal | 4 ± 2 | 5 ± 4 | 5 ± 3 | 5 ± 3 | 4 ± 3 | 4 ± 3 |
| Dominance | 6 ± 3 | 7 ± 2 | 5 ± 3 | 6 ± 2 | 6 ± 2 | 7 ± 2 |

Age was slightly positively correlated with the fear for COVID-19 (r=.21, *p*= .001) and with ASI-3 scores (r=.25, *p*= .001).

As a primary analysis of the efficacy of the audio clips, we performed a One-Way ANOVA on post-exposure relaxation scores. The analysis gave no significant differences between groups in perceived relaxation, after the exposure to the relaxing audio clips ($F$ (2, 237) =1.6, $p$ = .21).

To test and compare the efficacy between the audio clips, a Mixed ANOVA testing for group and time effect and their interaction was performed on perceived relaxation, perceived stress/activation, and preoccupations related to COVID-19.

All the effects reported below are stated as significant at $p < .001$ unless otherwise specified.

- *VAS relax*:

A significant moderate main effect for Time was found, $F(1,237) = 121.5$, partial $\eta^2 = .34$. Therefore, relaxation scores after the exposures were significantly higher than before listening to the audio clips. There was a non-significant effect of the group, indicating that the ratings from all the three groups were similar, $F(2, 237) = 1.15$, $p = .32$, partial $\eta^2 = .01$ Thus, there was no overall difference in the scores of perceived relaxations between Square Breathing, Body Scan, and Natural Sounds. Finally, findings revealed a non-significant Time x Group interaction, $F(2,237) = .32$, $p = .73$, partial $\eta^2 = .003$ (Figure 2).

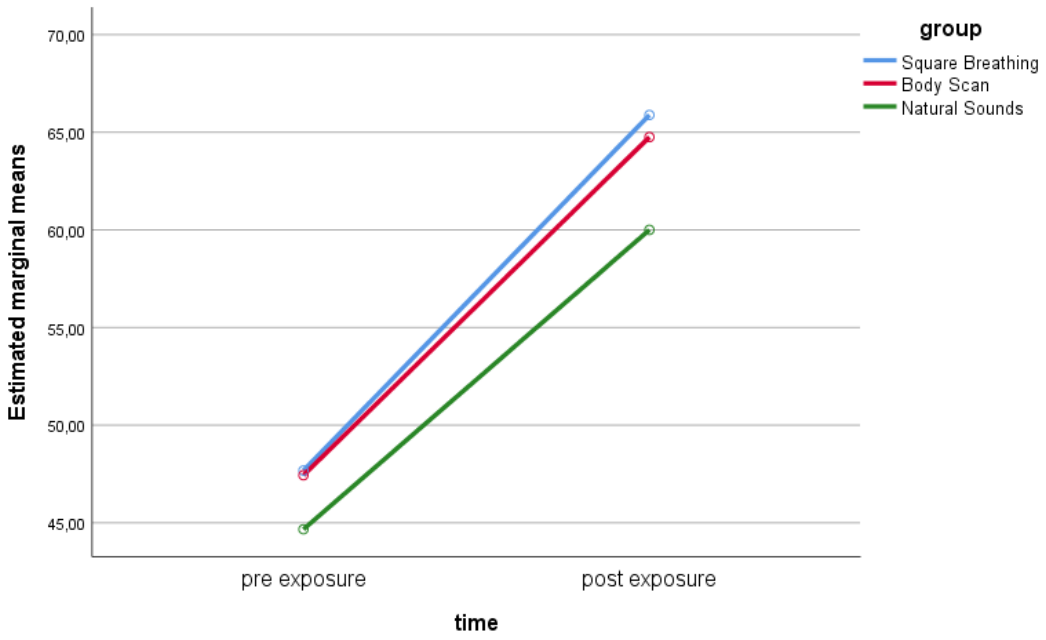


*Figure 2*: *Pre and Post VAS relax.* *Pre and post-exposure mean values of perceived relaxation in the three experimental groups*

- *VAS psychomotor activation/stress*:

A significant main effect of Time was found, $F(1,237) = 153.5$, partial $\eta^2 = .39$. Hence, perceived psychomotor activation/stress scores after the exposures were significantly lower than before listening to the audio clips. This effect was moderate. Results also showed a non-significant Time x Group interaction, $F(2,237) = .06$, $p = .95$, partial $\eta^2 = .0001$, while a small significant effect of the groups was found ($F(2,237) = 3.6$, partial $\eta^2 = .03$, $p$=.03). Contrasts between groups and post hoc tests revealed that the guided exercises yielded a lower level of perceived stress compared to the Natural Sounds.

Specifically, participants in the Square Breathing condition were significantly ($p$= .04) less stressed than the volunteers in the Natural Sounds group. Participants in the Body Scan condition rated their perceived level of stress as lower than the participants in the Natural Sounds ($p$= .03) (Figure 3).

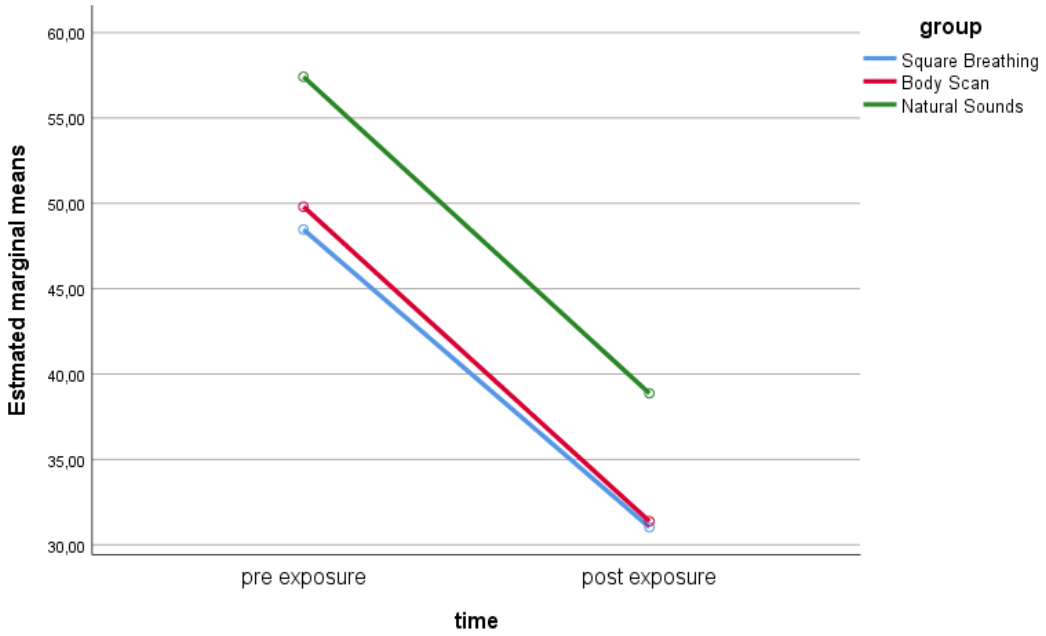


*Figure 3: Pre and Post VAS psychomotor activation/stress.* *Pre and post-exposure mean values of perceived psychomotor activation in the three experimental groups*

- *VAS fear related to COVID-19*

A significant main effect for Time was found, $F(1,237) = 103.4$, partial $\eta^2 = .3$. Therefore, the degree of fear for COVID-19 after the exposures was significantly lower than before the audio clips. There was a non-significant effect of the group, indicating that the ratings from all the three groups were similar, $F(2, 237) = .95$, $p = .38$, partial $\eta^2 = .01$ Thus, there was no overall difference in the scores of preoccupations related to the COVID-19 between Square Breathing, Body Scan and Natural Sounds. Finally, findings showed a non-significant Time x Group interaction, $F(2,237) = .37$, $p = .69$, partial $\eta^2 = .003$.

Overall, all three variables improved following the audio clips. Considering the differences between the groups, no significant differences emerged for perceived relaxation and the COVID-19 related preoccupation, while significant differences emerged in perceived psychomotor activation/stress, where the guided audio clips yielded a major decrease of perceived stress, compared to Natural Sounds (Figure 4).

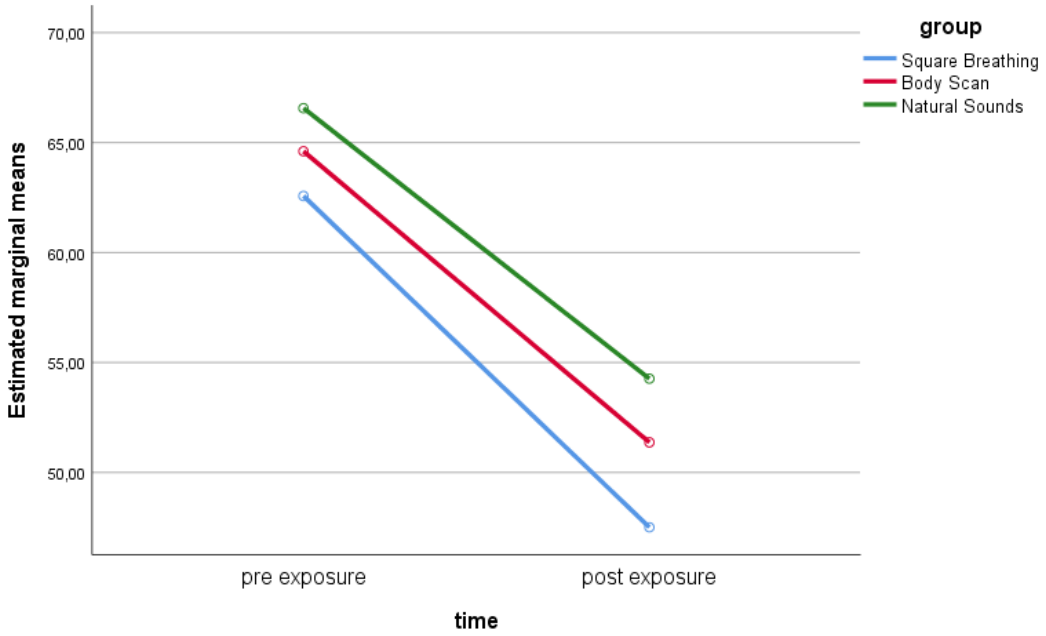


*Figure 4*: *Pre and Post VAS fear related to COVID-19.* *Pre and post-exposure mean values of thoughts related to COVID-19 in the three experimental groups*

*Emotional state (Valence, Arousal, Dominance)*

We performed nonparametric analysis on the SAM. To test if there was a difference in pre-post scores of the perceived emotional state, we run, for each experimental group, the Wilcoxon signed-rank test on variables assessed before and after the exposure to the audio clips. The effect sizes (*e.s.*) were reported in the form of Hodges and Lehmann effect size.

For all the groups, a significant improvement was observed on the dimensions of the pleasantness of the emotional state (valence) and perceived control over it (dominance), while a non-significant trend resulted in arousal.

For what concern the Square Breathing group, results showed a significant positive improvement in the valence (T= 640, z= 3.16, *p* =.002, *e.s.*= .5, 95%CI [0,1]) and in the perceived dominance (T= 477, z= 3.12, *p* =.002, *e.s.* = .5, 95%CI [0,1]), while a non-significant trend was found in perceived arousal (T= 707.5, z= 1.84, *p* =.065, *e.s.* = .05, 95%CI [0,1]). Considering the Body Scan group, again valence and dominance improved (T= 1045, z= 5.18, *p* =.0001, *e.s.* = 1, 95%CI [1,1.5] and (T= 393.5, z= 2.88, *p* =.004, *e.s.* = .5, 95%CI [0,1] respectively), while arousal did not (T= 516, z= .25, *p* =.804, *e.s.* = 0, 95%CI [-5,5]). Finally, the effects for the Natural Sounds group were significant for valence and dominance (T= 943.5, z= 3.70, *p* =.001, *e.s.* = .5, 95%CI [0.5,1], T= 516.5, z= 2.18, *p* =.029, *e.s.* = 0, 95%CI [0,.5]) and not for arousal (T= 457, z= .35, *p* =.728, *e.s.* = 0, 95%CI [0,1]).

To assess between-groups differences, we performed the Kruskal-Wallis test as a global test on the three groups. None of the comparisons between the groups yielded significant differences, thus we did not proceed with the paired comparisons.

Specifically, valence yielded to $\chi^2(2) = 4.6$, $p$=.1 at pre-exposure and $\chi^2(2) = 1.17$, $p$=.56 at post exposure, while arousal scores gave $\chi^2(2) = 2.56$, $p$=.28 and $\chi^2(2) = 2.17$, $p$=.34 respectively pre- and post-exposure, and analysis of dominance showed $\chi^2(2) = .18$, $p$=.91 and $\chi^2(2) = 1.25$, $p$=.54 as pre- and post-exposure differences.

*The moderation role of baseline anxiety on intervention efficacy*

To test if the levels of anxiety at baseline moderated the efficacy of the audio clips, we performed Mixed ANOVA, testing for moderation effects of the questionnaire scores STAI-

Y, ASI-3, BVS with group and time. The correlations between questionnaires and post-exposure scores are reported in Table 6.

Overall, there was a significant effect of the moderation between STAI-Y scores and Time ($F(1,234) = 7.22$, $p = .008$, partial $\eta^2 = .03$) on perceived relaxation. The same pattern was observed for the interaction with Time ($F(1,234) = 4.4$, $p = .037$, partial $\eta^2 = .02$) on psychomotor activation/stress, suggesting a greater efficacy for less anxious participants.

For what concern ASI-3, we found that there was a significant effect of the moderation between ASI-3 levels and Time ($F(1,234) = 4.3$, $p = .04$, partial $\eta^2 = .02$) on perceived relaxation, while a three-way interaction was found between Group, Time and ASI-3 for the effect on perceived psychomotor activation/stress ($F(1,234) = 3.2$, $p = .04$, partial $\eta^2 = .03$). For BSV scores, a significant moderation effect was found between BSV and Time ($F(1,228) = 5.4$, $p = .02$, partial $\eta^2 = .02$) on perceived relaxation. As for trait anxiety, these results suggested that the audio clips were less effective for participants with higher body vigilance anxiety.

*Qualitative results*

Qualitative answers on the subjective point of view were examined to understand the subjective experience and to discover possible ameliorations of the proposed stimuli. Within the discussion, practical advice for future studies is given accordingly.

Firstly, six different categories for participants' relaxing preferred activities were identified. Most of the participants reported more than one way to achieve a state of relaxation. Physical activities (172/330) and hobby (130/330) were identified as the most common practices to feel relaxed: people like to go out for a walk or play sports, while others prefer to spend their spare time listening to music, watching films, or reading. Participants also liked to relax by fostering social relationships and being with pets (80/330), taking care of themselves (24/330), traveling (14/330), and meditating (11/330).

Then, participants were asked to identify the pro and cons of the proposed relaxation exercise. Most of them liked the audio features (83/240), such as the teacher's recorded voice

or the sound of water (if present). Participants also loved the sense of relaxation (49/240) or awareness (14/240) they achieved after practicing the exercises. Some participants got the opposite hoped impact, and they became bored by the recorded audio.

Finally, few participants left suggestions. Precisely, they would vary the length of the intervention and give more instructions during the guided exercises.

### *2.4.3 Discussion*

#### *Clinical Implications*

People are facing the COVID-19 pandemic worldwide. The fright influenced citizens' lives, leading to an increase in stress levels. Moreover, the lockdown forced people into a social isolation condition and stopped the realization of in-person programs to target psychological problems. Notably, in our sample, which was composed of Italian citizens under social distancing restrictions, anxiety was slightly enhanced compared to normative data.

In such a situation, effective intervention for stress and anxiety management becomes increasingly difficult to be implemented. However, remote interventions have been increasingly adopted in clinical practice, by facilitating psychological assessment and enabling the delivery of treatments to many subjects concurrently (Andersson, 2016).

The present randomized study provided data on the effectiveness of remotely delivered interventions with natural sounds, deep breathing, and meditation practice on perceived relaxation, psychomotor activation, level of preoccupation associated with COVID-19, and emotional state. It also shed light on if and to what extent one of these exercises can provide greater benefits compared to the others. Indeed, a comparison among natural sounds, respiration, and body scan meditation techniques in internet-based interventions was missing in the literature.

In accordance with our first prediction, results showed that all three techniques were effective. Specifically, we found that perceived relaxation levels, psychomotor activation/stress, and disturbing thoughts related to COVID-19 significantly improved after

the three audio clips, with a moderate effect. Considering this evidence, we concluded that the audio clips were effective in inducing a calmer psychological state. Our findings are consistent with the results from another study aiming at reducing anxiety and depression in patients with COVID-19. The study provided a remote intervention with breath relaxation training, mindfulness body scan, and behavioural techniques. The techniques significantly improved mood disturbance symptoms (Wei et al., 2020).

Considering between groups' differences, results showed significant variations only on perceived psychomotor activation/stress, where guided exercises (Square Breathing and Body Scan) resulted to be more effective than the Natural Sounds audio clip. No other differences in efficacy between groups were raised. These findings partially confirmed our second hypothesis, as we obtained enhanced efficacy only on the dimension of stress and not on the perceived relaxation.

We concluded that, for this brief remote relaxation intervention, the three audio clips were effective in improving psychological adjustment. We speculated that, even if the audio clips involved different psycho-cognitive activities (the regulation of breath frequencies, the awareness of body sensation, and the listening to natural sounds), for brief relaxation experiences, these different processes do not determine significant variations in efficacy. Thus, for simple and brief interventions, all three can be effectively applied. Consistently, Jain and colleagues (Jain et al., 2007) conducted a randomized controlled trial on the differences among mindfulness meditation, relaxation training, and a waitlist control group in reducing distress. No statistical differences were found between the two treatment groups, even if both interventions significantly improved the emotional state and reduced the distress.

Furthermore, regarding differences between groups, we hypothesized the guided exercises to be more effective compared to Natural Sounds in perceived stress, since they require users to bring their attention to body sensations and breathing frequency, promoting calm states, without trying to change thoughts. A systematic review on the importance of guidance

during remote interventions showed that guided interventions are more effective than non-guided ones (Baumeister, Reichler, Munzinger, & Lin, 2014). Instructions may not change the degree of muscle contraction or the perception of the body, but rather they can endorse a state of pleasant awareness, which is in line with the purpose of meditation practices. Participants stated the audio clips made them stop the preoccupation and think about their breathing rhythm. Others told they had the opportunity to look at their "inner world", getting calmer. Furthermore, audio features may influence the pleasantness of the audio clips. Most of the participants reported positive feelings and a sense of relaxation due to the registered voice, while others disliked the tone of voice, got bored, or became hyperactive or upset.

For what concerns the emotional state, assessed through the SAM, we found that all the audio clips were effective in improving the valence (pleasure) of the emotional experience and the perceived dominance over it. No significant results were found on the dimension of the degree of arousal related to the emotional state. Based on these latter results, we speculated that the relaxing audio clips were more effective in enhancing the pleasantness and the feeling of being in control with one's emotions, rather than the activation linked to such an emotional state.

This study provides data that can orient the development of future low-cost remote interventions to reduce preoccupation and anxiety in the general population. Future studies might also assess and compare the efficacy of these approaches in clinical protocols for patients struggling with anxiety and hyperarousal.

*Limitations and future directions*

The study presents some limitations.

First, it employed single-session guided interventions. Thus, we could not evaluate differences in the efficacy of prolonged exposure to relaxation sessions or correct for the effect of training or habituation. However, our study demonstrated that even a very brief online intervention can contribute to a momentary, yet significant stress reduction. Future studies might adjust the length of the audio clips also in the light of the participants' reports.

A second limitation of the present study is that we employed only self-reported measures. Indeed, as our intervention was delivered in a context of social distancing, other approaches were impossible to implement. However, future studies with more objective measures and psychophysiological variables (such as skin conductance or heart rate variability), would strengthen the evidence of the efficacy of these techniques.

Third, we enrolled a convenience sample with online recruitment. For this reason, we kept the inclusion criteria a little bit vaguer, compared to face-to-face enrolment.

Finally, considering the possibility of applying this kind of intervention also to a clinical population, future studies might also deepen the relationship between individual differences and the efficacy of the techniques.

In the present study, we included trait anxiety and the levels of anxiety related to bodily sensations. However, we could not perform a complex moderation model, nor we could conclude how different levels or different types of anxiety might shape the efficacy of the techniques. Partial preliminary evidence from moderation effects seems to point out a moderation role of anxiety.

# 3. Empirical contribution: Relaxation interventions for cancer patients

## 3.1 *Introduction to the research studies*

Cancer patients might display peculiar needs and preferences, which might vary according to the phase of the treatment, personal preferences, and past experiences.

Thus, cancer patients deserve specific studies to collect data that might inform future tailored interventions.

The following studies were conducted with quantitative and qualitative approaches and they aimed at collecting information on the cancer patients' preferences about the features of the stimuli to be used in digital relaxation.

Thus, the studies were focused on the evaluation of the features of the digital stimuli to be used in relaxation (visual and auditive contents), and on the possible techniques to be paired with such contents.

Specifically, the aims of the studies were to 1) gather information about hospitalized cancer patient's preferences for digital relaxing contents, 2) pilot testing a specific virtual scenario, to be used in future studies 3) test and compare the efficacy of guided relaxation techniques paired with a specific VE.

### *3.2 User-centered design on hospitalized cancer patients*[3]

*Overview*

The present study aimed at adding knowledge on cancer patients' preferences on the tools which can be employed in the field of VR interventions for relaxation.

Specifically, the study was conducted on cancer patients which were in a specific phase of the care flow process: the post-surgery hospitalization.

Indeed, Hospitalized Cancer Patients (HCP) can face distressing psychological and physical conditions, and VR for relaxation might offer benefits to this target of patients. To date, no prior study inquired on the specific patients' preference and opinion regarding this possible intervention.

The present contribution might provide initial data on the patients' preferences on possible tools to be employed in VR for relaxation in hospitalized cancer patients. For this scope, according to user-centered methodology, a qualitative approach was applied.

We interviewed HCPs to assess 1) if and to what they would like to receive such an intervention, 2) which contents they would like to be presented with for relaxation.

*Background*

VR may be used to relax and distract HCPs, which confront several distressing moments during the care flow process (Carlson et al., 2019; Zebrack et al., 2015).

From the initial studies that applied technological and digital tools on cancer patients ( Oyama et al., 1999; Oyama, 1997), VR has been employed to target different clinical effects (distress, nausea, pain, etc) within the field of cancer care (Chirico et al., 2016).

However, there is a high variety of VR interventions for cancer patients. Indeed, VR interventions targeted heterogeneous patients and clinical variables. A specific evaluation of the applications of VR tools on psychological issues among cancer patients is difficult.

[3] Adapted from Pizzoli, S.F.M, Marton, G., Vergani, L., Monzani, D., Mazzocco, K., Kufel, E., Pravettoni, G. *Virtual reality for relaxation for hospitalized cancer patients: tailor digital intervention on patients' needs*. Oral presentation; IPOS 2021.

Notably, HCPs should be considered as a peculiar target for VR, as they usually display specific physical and psychological needs, related for example to post-surgical conditions or specific side effects of the therapies.

Relaxation is a promising approach to relieve pain and distress for those patients (De Paolis et al., 2019). However, to date, an explicit evaluation of HCP's preferences regarding VR for relaxation during the hospitalized period is lacking in the literature.

Thus, a study focused on their peculiar needs and preferences might shed light on the construction of future personalized approaches, personalized according to their specific requirements.

In the present study, we aimed at collecting information to tailor VR features for HCPs, via qualitative inquiries on patients' needs and opinions about receiving VR for relaxation in hospital.

For this scope, HCPs were presented with templates of virtual scenarios and interviewed following a semi-structured interview.

### *3.2.1 Material and methods*

*Participants and procedure*

14 HCPs took part in the study and were interviewed according to a semi-structured interview.

Overall, the mean age was 54.6 (*s.d.*: 14.3, age range: 29-75); 6 (42.9%) were women, 8 (57.1%) men. The education level counted in years was 13.7 (*s.d.*: 3.9). Considering cancer type, 11 had urogenital cancer, while 3 had breast cancers.

Participants were included if they were 1) Italian or proficient Italian speaker; 2) did not present audiovisual disturbs; 3) did not suffer from relevant pain at the time of the interview. Patients were informed about the scope of the project and received a brief definition of what VR is.

Participants were at first asked to figure out which digital contents they imagined they would like to be presented with, to reach relaxation, and what they usually like to do to relax in daily life. Then, four 360° VR scenarios (See Figure 5) were showed to each participant. Participants had to comment on positive-negative aspects and choose a favorite scenario.

The scenarios were composed of digital 360° scenes, which could be sawn with a Smartphone Nexus 5x©. The scenarios were 1) a mountain viewpoint from a rounded balcony of stone (Balcony), 2) the internal of an ancient cathedral (Cathedral), 3) a path into a red forest (Forest), 4) a seaside at sunset (Seaside). Moving the smartphone, participants could have a 360° view of the virtual landscapes.

The four scenarios differed from each other for features such as the contents (natural/with architecture), the tone of the colours (warm/cold colours), the point of view of the user (high viewpoint/grounded position), and the presence of water (no water/ water) (Table 8). After every scenario, subjects were asked to tell what they liked or disliked and what they would have changed in the scenarios.

Table 8: *Features of the four digital scenarios*

| **Features** | **Scenarios** | | | |
|---|---|---|---|---|
| | ***Balcony*** | ***Cathedral*** | ***Forest*** | ***Seaside*** |
| ***Contents*** | With architecture | With architecture | Natural | Natural |
| ***Tone of colours*** | Cold | Cold | Warm | Warm |
| ***Point of view*** | High viewpoint | Grounded position | Grounded position | Grounded position |
| ***Presence of water*** | No | Yes | No | Yes |

The order of presentation of the scenarios was randomized across subjects and participants were instructed and guided on how to use the smartphone and visualize the scenarios.

Finally, patients had to express their opinion on the utility of VR for relaxation during hospitalization and to state when they would have received such an intervention.

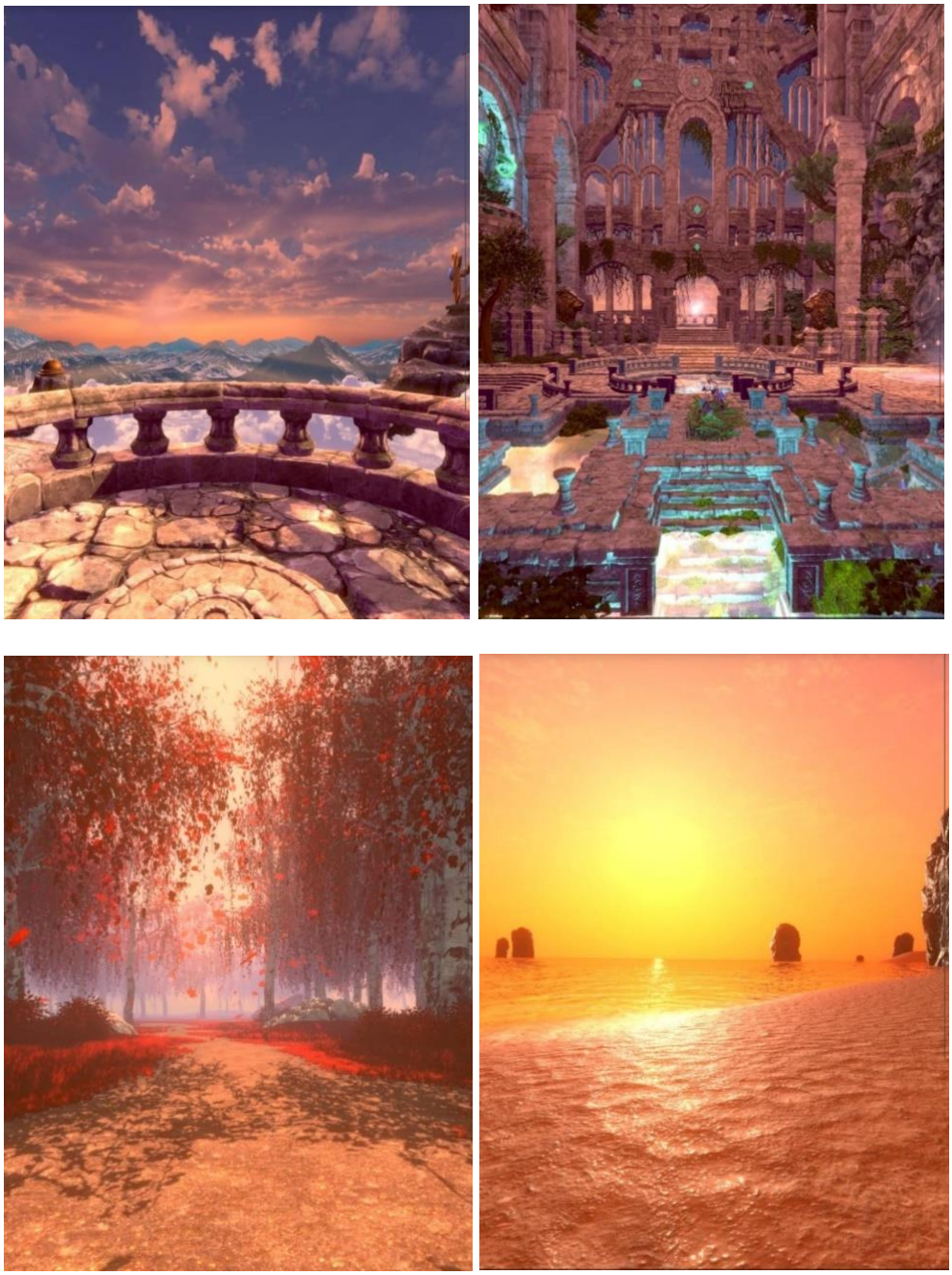

*Figure 5*: *The virtual scenes*[4]. The 360° scenarios (1. Balcony, 2. Cathedral, 3. Forest, 4. Seaside).

### *3.2.2 Results*

Overall, there was a fair heterogeneity among VR imagined preferred contents. Participants reported different preferences on the perceptual features (colours, closed-open environments) and on the stimuli (animated, autobiographical) they would put in VEs.

[4] The original version of the virtual environments used in the study were developed by Prosoma Digital Therapeutics, a company working on immersive technologies for applications in psycho-oncology.

8 out of 11 participants preferred natural scenarios (sea, mountains, grass), while, for what concerns the specific stimuli to be inserted inside the VE, they would like to hear water (3) and nature (5). Overall, 7 respondents highlighted the importance of having pleasant auditive stimulation. 2 participants said they would choose to see their autobiographical memories inside the VE, while one said that he would have seen other people inside the VR. Interestingly, 5 participants reported that they would ask for animals to be inserted into the VE.

As regards the comments on the four scenarios, we found that natural scenarios were preferred by almost all the participants, except for two, who showed a preference for the first and the second scenario ("*I am an architect and I like cathedrals*").

The most disapproved features were the lack of reality of the scenes (unreal colours or unreal architectural structures, *"it is not realistic"*; "*it seems a videogame and I do not like it"*) and the presence of the colour red in the two natural landscapes ("*it is not the colour of the sea*"). Specifically, red was negatively commented since it was not a realistic colour for the sea or the forest, and because of its association with blood. A young woman said *"it reminds me of blood, it makes me think about the surgery and the pain"*, while another woman told, "*you should not use red, it is too strong and it is the colour of blood and I do not want to think about my blood".* The different points of view of the scenes were commented only by a subject, who appreciated the first scenario as it was a panoramic point of view. He also disliked the second one, because it gave him the sensation of being small and in a low position.

For what concern the changes participants would have made to the four scenarios, the main suggestions were to 1) put animals inside the scenarios, 2) add interaction with animated stimuli, 3) use real places (for example famous Italian squares), and 4) give the possibility of adding autobiographical stimuli.

Notably, most of the participants (11) considered a VR intervention for relaxation as useful for people in their situations and themselves, while two stated that they would not like such an intervention, and one felt he was not able to give an opinion on it.

The 11 who did recommend this type of intervention thought that considering their experience, VR for relaxation would be useful the most during the waiting phases after surgery, the recovery (9), and during chemotherapy (2).

### *3.2.3 Discussion*

The majority of HCPs considered VR for relaxation as useful. They reported that they would have received it mainly during the waiting period inside the hospital or after surgery.

Considering the comments on what patients would like to see in VE and on the showed VEs, we concluded that natural environments should be preferred the most, with specific attention on the sounds to be inserted in the scenarios.

More importantly, it should be granted the possibility of having a library of stimuli and features, that patients can utilize to personalize their own environments.

Indeed, participants expressed heterogeneous preferences mostly for what concerns the reality of the scene (digital or real-life scene) and the contents (autobiographical stimuli, animals, real places). The possibility to interact with virtual content should be modulable too, to meet users' preferences.

Moreover, results pointed out the fact that specific HCPs' psychological needs and preferences should be systematically addressed before the construction of VR interventions, as highlighted by the comments on the red features of the environments. The user-centered design approach might provide a valuable method in this direction.

For example, we hypothesized that red was a negative element because of its association with blood, as we tested patients who were in a specific phase (after surgery).

The preferences for the specific phase of the treatments in which patients would receive the interventions, if they want to, should also be carefully assessed.

Overall, such results should stress the importance of a careful assessment of users' preferences before the real interventions.

*Limitations and future directions*

The present study presents some limitations which should be carefully considered.

Firstly, the study was conducted on patients with heterogeneous cancer types and that were hospitalized after surgery. Consequently, these results provide only preliminary data on the possible preferences of the participants.

Indeed, these results should not be considered as generalizable to all cancer patients or patients in different stages of the care flow process. Moreover, the results should not be considered as associated with a specific cancer type.

Furthermore, participants were asked only for the evaluation of the scenarios and for their opinion and preferences on VR in the hospital. Other types of preferences might be elicited in future studies.

Participants also saw the scenario only through a smartphone and not with an immersive modality. Consequently, we could not draw inferences on the efficacy of the scenarios in inducing a sense of presence in the users.

Lastly, we did not present scenarios with characters or avatars. So, we could not specifically evaluate the preference for the interaction with an avatar inside the VEs.

Furthermore, the type and the characteristics of the autobiographical stimuli and avatars should be further addressed in future studies.

### *3.3 The waterfall environment*[5]

*Overview*

The present study presents a pilot test on the relaxation properties of a VE meant to be used for relaxation interventions for cancer patients.

Specifically, the relaxation properties of a Waterfall VE, which was used in the study on breast cancer survivors (Tailoring relaxing experience on breast cancer patients: a pilot study) was tested in a pilot study on healthy subjects.

To assess the relaxation properties, a quantitative approach was employed. Psychological and psychophysiological measures were evaluated before and after the exposure to the Waterfall Environment, to assess the impact of the experience with the scenario.

The results gave initial data on the efficacy, in terms of relaxation, of the visual and auditory components of the digital environment.

*Background*

The present work is a part of a project that aimed at testing the impact of arousal modulation, carried out with two VEs (high arousal and low arousal), on memory efficiency.

Here is described the part of the work dealing with the properties of arousal modulation of a specific environment, the Waterfall Environment.

In the original work, participants were enrolled and randomly assigned to two experimental groups: a high arousal group, which saw a VE with a roller coast, and a low arousal group, which received a natural landscape environment with realistic sounds. Both the groups, before using the VR, underwent a memory task, that will not be reported here.

In the natural landscape condition, participants were asked to stay immersed in a 360° digital environment representing a waterfall with a luxurious forest (Figure 6). The entire exposure lasted four minutes and during that time, volunteers heard nature associated with the

[5] Partially adapted from "The Role Of Arousal In Memory And Learning Performances: A Virtual Reality Approach"; Master Thesis; Luca Raggio, MSc. Relator: Prof Ketti Mazzocco; Correlator: Silvia F. M. Pizzoli.

environment (birds singing, the wind, the sound of the waterfall). The VE started with a natural path which ended with a waterfall landscape. Initially, the viewpoint automatically made the user walking through the path, until the waterfall landscape.

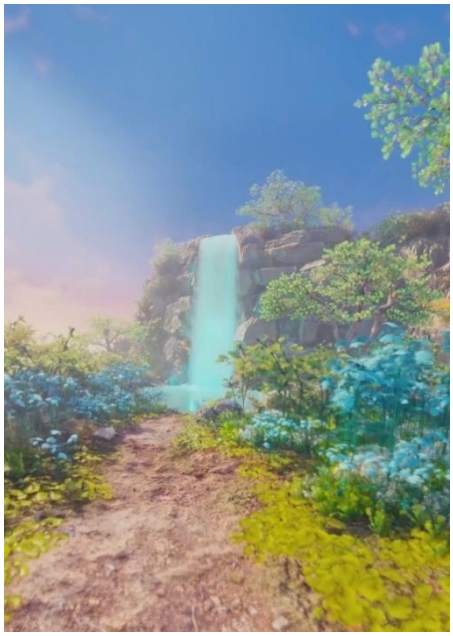

*Figure 6*: *The Waterfall environment*[6]. *A frame of the Waterfall environment*

Through this simple exposure, we could assess the impact of the experience of the Waterfall Environment on some dimensions related to perceived relaxation (subjective state) and psychophysiological activation (objective state).

The subjective perceived psychological state was assessed with the request of rating the degree of relaxation and arousal felt, as well as requiring participants to evaluate their emotional state, before and after the experience with the environment. Specifically, perceived relaxation and arousal were assessed through Visual Analogue Scales (VAS), while the emotional state was rated on the three dimensions of the Self-Assessment Manikin (SAM). The subjective measures employed in the study are used in literature for detecting

[6] The original version of the virtual environment used in the study was developed by Prosoma Digital Therapeutics.

changes in perceived arousal (Brown & Ryan, 2003; Littel, Remijn, Tinga, Engelhard, & van den Hout, 2017).

As a measure of the objective psychophysiological state, this study used heart rate, for its easiness in data collection and interpretation and its strong literature validity as an arousal assessment procedure (Azarbarzin, Ostrowski, Hanly, & Younes, 2014). Furthermore, heart rate is used in literature for VR-induced arousal assessment (Ham, Cho, Oh, & Lee, 2017; Peterson, Furuichi, & Ferris, 2018).

### *3.3.1 Materials and Methods*

*Participants and Procedure*

27 healthy volunteers, which met the criteria of 1) age range 18-35; 2) Italian native speaker or Italian proficient speaker; 3) agreed and signed written informed consent, were enrolled. The following exclusion criteria were applied:1) Presence of blindness or severe sight loss; 2) Presence of deafness or severe hearing loss; 3) Presence of any serious medical, neurological, or mental disorder; 4) History of alcohol or drug abuse.

After giving the written informed consent, the participants were screened for exclusion criteria, and if none were present, they were given a questionnaire including sociodemographic variables. Before and after the exposure to the VEs, self-reported questionnaires were administrated.

Before the exposure, participants were instructed to use the head-mounted device (VR HUD). They were subsequently asked to stay for a 4-minute period with the eyes closed, for the recording of the basal heart rate (baseline). After the measurements of the heart rate baseline, subjects were asked to complete the VAS scale on perceived relaxation and arousal activation and the SAM questionnaire. Post-exposure they were asked to re-fill the same self-reported questionnaires, and a VAS scale on presence.

Subjects were randomly assigned in two conditions: one called Low Arousal (Waterfall Environment, N= 14) and the other High Arousal (Roller Coast, N= 13).

For experiencing the VR, a Shinecon VR 2.0 HUD was provided. The device chosen for the video was a Xiaomi Redmi Note Pro 8, with a 6.53inches, 1080X2340 pixels resolution, and 395 PPI density.

*Measures*

Sociodemographic variables included age, gender, marital status, education, employment, alcohol and tobacco consumption, physical activity, use of glasses, computer, and VR technology knowledge.

Self-reported questionnaires comprised the Self-Assessment Manikin (SAM) and two 100 mm length Visual Analogue Scale (VAS), for evaluation of relaxation and activation.

The SAM is a 9-point Likert scale non-verbal pictorial scale that directly measures the degree of pleasure, arousal, and dominance, associated with the emotional reaction to a certain stimulus. The SAM depicts a smiling, happy figure to a frowning picture when representing the Valence dimension (i.e.: the pleasantness of the emotional state), an excited, wide-eyed figure to a relaxed, sleepy picture for the Arousal dimension (the activation linked to the emotional state) and it depicts the Dominance with different sizes of the manikin, where a larger figure indicates more control over the situation (Bradley & Lang, 1994).

Before and after the VE, the subjects compiled the SAM, and the 3 VAS (presence, relaxation, and arousal).

The subject heart rate was recorded prior, during, and after the VE.

Heart rate was collected with an optical heart rate sensor: the device shines green light (of a specific wavelength) from a LED through the skin, measuring how it scatters off the blood vessels.

For this study, the low-cost, open-source PulseSensor by Pulsesensor Inc. was chosen. The device had a 500 Hz-possible sample rate and a beat-to-beat timing resolution of 2mS with a consumption rate of 4 mA. The data of the PulseSensor was recorded by a microprocessor, namely Arduino Uno.

*Statistical Analysis*

For the present work, only results on pre-post differences in arousal, relaxation, SAM dimensions (valence, arousal, dominance), and heart rate are reported.

The post-exposure VAS on the sense of presence in the low arousal group is described too, while the heart rate values were compared between baseline and post-exposure.

Data were analyzed with a nonparametric approach. To test if the levels of arousal, relaxation, SAM dimensions, and heart rate were modified by the exposure to the Waterfall Environment, we performed a Wilcoxon signed-rank test on the Waterfall group. The effect sizes (*r*) are reported too. The data were analyzed with SPSS version 26.00.

*3.3.2 Results*

Among the participants enrolled in the Waterfall Environment (N=14), 10 (71.4%) were male and 4 (28.6%) females, while for what concerns marital status, 13 (92.9%) were single, 0 (0%) cohabitant, and 1 (7.1%) married subject. 6 (42.9%) had a high school degree, 6 (42.9%) had a bachelor's degree, and 2 (14.2%) a master's degree. For what concerns alcohol consumption 5 (35.7%) subjects stated that they never drink, 2 (14.3%) one time per week, 6 (42.9%) 3-5 times per week, and 1 (7.1%) used to drink daily. As regards smoke habits, 5 (35.7%) did not smoke, 2 (14.3%) smoked occasionally and 7 (50%) smoked daily. For the physical activity, 3 (21.4%) of subjects did not practice physical activity, 5 (35.7%) did it one time per week, 3 (21.4%) 3-5 times per week, and 3 (21.4%) exercised every day. As regards computer knowledge, 2 (14.3%) subjects declared no experience, 3 (21.4%) declared a low level, 4 (28.6%) an average level, and finally, 5 (35.7%) stated an expert level. 10 (71.4%) of the volunteers did not have prior experience with VR and 4 (28.6%) had previously tried it.

Considering the sense of presence, participants after the Waterfall environment scored a mean of 52.93 points (*s.d.*= 15.52) on the VAS scale (a fair degree of presence).

Differences in the pre-post perceived levels of relaxation and arousal, in the SAM dimensions, and heart rate are reported in Table 9.

Table 9: *Differences pre-post exposure in subjective and objective measures*

| *Measures* | *Pre-exposure* | *Post-exposure* | *Wilcoxon signed-rank test* |
|---|---|---|---|
| Relaxation (VAS) | *Mdn*= 34 | *Mdn*= 48 | T= 94, z= -2.61, *p* =.009*, r= -.7 |
| Arousal (VAS) | *Mdn*= 39 | *Mdn*= 37.5 | T= 43, z= -.175, *p* =.86, r= -.05 |
| Valence (SAM) | *Mdn*= 5 | *Mdn*= 6 | T= 88, z= -3.01, *p* =.003*, r=-.08 |
| Arousal (SAM) | *Mdn*= 5 | *Mdn*= 4 | T= 3, z= -.2.71, *p* =.007*, r=-.72 |
| Dominance (SAM) | *Mdn*= 5 | *Mdn*= 5 | T= 33, z= -.2.16, *p* =.03*, r=-.58 |
| Heart Rate | *Mdn*= 70 | *Mdn*= 61.5 | T= 105, z= -.3.30, *p* =.001*, r=-.88 |

Overall, except for perceived arousal, all the psychophysiological variables improved after the Waterfall environment. Specifically, relaxation levels improved, the pleasantness (valence) and perceived control (dominance) of the emotional state increased, while the mean of the heart rate decreased from the baseline to the end of the exposure.

The effect sizes from all the measures ranged from .08 to .88. The stronger effect involved the heart rate (objective measure), the perceived dominance of the emotional state, the degree of activation (SAM), and the perceived relaxation (subjective measures).

*3.3.3 Discussion*

This pilot study showed that the use of the Waterfall environment can alter both physiological and self-reported measurements with statistically valid results, including robust effect sizes, in the hypothesized directions.

Indeed, almost all the psychophysiological variables improved after the exposure to the Waterfall environment, with the only exception of the perceived level of arousal on the VAS scale.

According to the analyses and the effect sizes, the improvements were significant and with a medium-strong effect. The objective measure (heart rate) showed a greater improvement ($r$= .88).

Consistently with the physiological measure, considering the subjective perceived states, the VE improved the level of relaxation, the pleasantness of the emotional reaction and the control participants felt over their emotional reactions.

Overall, these results pointed out that this specific Waterfall Environment can be effective in inducing relaxation and in improving psychophysiological states in young healthy subjects.

*Limitations*

These results should be interpreted with caution.

First, the sample size of the study was small and there were no comparison groups.

Furthermore, we tested only the visual and auditory features of the environment, without specific narratives or interactions with virtual stimuli. Similarly, we did not compare the scenario with different lengths.

Consequently, the results are strictly linked to this simple version of the environment.

As regards the objective measures, heart rate might be not sufficiently informative on the arousal state. Other physiological indexes should be included in future studies (skin conductance, heart rate variability), to further address psychophysiological changes.

Lastly, subjective were not asked for qualitative descriptions of their experiences. Thus, we could not understand if some specific features helped participants to reach relaxation.

### *3.4 Tailoring relaxing experience on breast cancer patients: a pilot study*[7]

*Overview*

The scope of this step of the project was to test the suitability of specific virtual relaxation techniques for cancer patients.

Specifically, the aims were to compare the efficacy of two broadly used relaxation techniques (respiration control and body scan) virtually delivered and ask for patients' experience with them.

To explore the specific preferences of this type of user, in the present project, the same VE was integrated with audio narratives designed according to two different relaxation techniques.

As an initial exploration, breast cancer survivors were exposed to the two versions of the VE, to evaluate the effectiveness, pleasantness, overall satisfaction with the technique and sense of presence, as well as the impact on the emotional dimensions of valence, arousal, and control. The aforementioned variables were evaluated by questionnaires and analyzed with a quantitative approach.

Furthermore, to tailor future virtual interventions for cancer patients, participants were asked for narrative descriptions of the experience with the relaxing VR and on the comparison between a relevant autobiographical memory of relaxation and the VR experience. For this last step, consistently with the user-centered approach, a qualitative methodology was employed.

*Background*

A growing body of evidence demonstrated that VR can be used to promote relaxation, stress relief, and even to train emotion regulation abilities (Baños et al., 2012; Villani, 2006; Villani, Riva, & Riva, 2007a). This is related to the possibility, inherent to VR, of

[7] Adapted from Pizzoli, S. F. M., Triberti, S., Monzani, D., Mazzocco, K., Kufel, E., Porebiak, M., & Pravettoni, G. (2019, June). Comparison of relaxation techniques in virtual reality for breast cancer patients In 2019 5th Experiment International Conference (exp. at'19) (pp. 348-351). IEEE; and from Pizzoli, S. F. M., Triberti, S., Monzani, D., Mazzocco, K., Kufel, E., Porebiak, M., & Pravettoni, G. Virtual reality for relaxation: tailoring digital experiences on breast cancer patients. IPOS 2019. Banff, Canada.

“substituting” the user experience with a digital, immersive environment, with multi-sensorial stimulation (Slater, Spanlang, Sanchez-Vives, & Blanke, 2010). To date, most studies that evaluated the effectiveness of VR for relaxation involved healthy participants and focused on experimental VEs and/or prototypes of products meant for healthy individuals. However, interest is growing towards using relaxing VR tools in healthcare contexts, such as cancer (Bani Mohammad & Ahmad, 2018; Rosa M Baños et al., 2013; Indovina et al., 2018; Schneider & Hood, 2007).

As recognized by the American Psychiatric Association, a cancer diagnosis can be a traumatic event, which generates serious consequences in terms of negative cognitions, emotions, and mood (Cordova, Riba & Spiegal, 2017). Patients may develop depression, pathological anxiety, and stress-related to the disease and the issues related to treatment management. Anxiety and stress are influenced by physical (e.g., age, hormonal changes, side effects of treatment), and psychological factors (e.g., negative feelings about the disease, and the resistance to change one’s lifestyle to adhere to treatment prescriptions) (Lim, Devi, & Ang, 2011). Breast cancer in particular, besides being the most common cancer in women worldwide, representing 25% of all cancers (Lahart, Metsios, Nevill, & Carmichael, 2015; Oeffinger et al., 2015), is characterized by illness-specific stressors. Indeed, the treatment often implies significant alterations of body image (ranging from skin discoloration, dermatitis to hair loss and disfigurement of one or both breasts) and related psychological issues in individual and social/intimacy well-being.

For this reason, it is important to test innovative tools for promoting relaxation in patients, to evaluate not only tools’ overall functionality, but also their adequacy to patients’ experience and needs, as well as to identify the best practices for designing technologies suited for inclusion in the psychological treatment prescriptions.

Typical VR interventions for relaxation usually employ natural scenarios, which are considered relaxing per se, and narratives inspired or directly derived from traditional relaxing techniques (e.g. autogenic training, meditation, respiration control, and so on)

(Anderson et al., 2017; Annerstedt, Jönsson, Wallergård, Johansson, Karlson, Grahn, Hansen, & Währborg, 2013).

The aforementioned techniques, when integrated into immersive VEs, can be used in a variety of ways: as stand-alone narratives, mixed with each other, combined with natural sounds, or can be coordinated with interactive contents within VEs. Some of these techniques, mainly centered on the control of body functions, instruct the user to maintain a specific breathing frequency, to gain awareness of the states of the body, and to perform muscular contraction and release exercises (Bishop et al., 2004; Scheufele, 2000). Others instead include explicit instructions to gaining control over mental state and letting go of negative thoughts. Notably, most of these methods are "training" to learn to reach relaxing or peaceful states, rather than being a one-shot treatment.

Even if putting in VR narratives inspired to those approaches has been proved to be effective in several contexts, little is known about which techniques or which combinations of techniques are effective the most on cancer patients.

As a step in this direction, in the present study, a VE designed to promote relaxation in cancer patients has been modified in two versions, featuring narratives with exercises based on two different techniques for relaxation: a breathing control exercise derived from yoga practices, and a body scan exercise, guiding users' attention towards body perception (Mirams, Poliakoff, Brown, & Lloyd, 2013; Sauer-Zavala, Walsh, Eisenlohr-Moul, & Lykins, 2013). These two VEs were tested with women who had breast cancer and underwent treatment, for the purpose of gaining information on the efficacy of the two exercises and the subjective experience with them. Such information indeed will inform the future development of VR relaxation tools for breast cancer patients.

Furthermore, to tailor virtual interventions for breast cancer patients, participants were asked for qualitative answers 1) on the experience with the relaxing VR and 2) on the comparison between a relevant autobiographical memory of relaxation and the VR experience.

### *3.4.1 Materials and Methods*

*Participants and Procedure*

16 breast cancer patients (age M: 47.7, s.d.: 7.24; education level M: 15.7, s.d.: 2.6) took part in the study. 4 of them had previous but limited experiences with VR technologies (e.g., trying it at art exhibits), while 12 of them previously tried relaxation-related practices and techniques (mostly yoga disciplines). All the participants except one were workers.

*Tools*

The hardware equipment was as follows: Smartphone Nexus 5x©, iHarbot© head-mounted display to be used with the smartphone; headphones connected to the smartphone for audio. Software equipment for the VE was a full 360° animated scenery developed in Unreal Engine© and representing a natural landscape with a high waterfall (Figure 7) and colorful plants and flowers (the Waterfall VE henceforth).

The Waterfall VE was integrated with two different audio narratives told by a male voice belonging to a qualified yoga and mindfulness instructor, helping the user to perform relaxation exercises. The first narrative guided users in controlling the breathing frequency, while the second followed the body scan method, bringing attention to physical sensations.

Indeed, previous studies demonstrated that the interventions based on respiration and meditation help individuals to alleviate the effects of stress, by reducing physiologic arousal and restoring autonomic balance (Rainforth et al., 2007; Thoma, Mewes, & Nater, 2018; Wielgosz, Goldberg, Kral, Dunne, & Davidson, 2019).

Furthermore, audio clips with instructions for muscle relaxation already proved to be effective for improving well-being in cancer patients (Holland et al., 1991).

Both the narratives lasted 7 minutes and were written to be as similar as possible in terms of number and length of unique sentences.

*Procedure*

Participants entered the psychology laboratory and were greeted by a female experimenter. After they signed informed consent to participate in the study, they were invited to try on

the head-mounted display and watched a neutral 360° image to familiarize themselves with the VR experience. The research was conducted according to the Declaration of Helsinki and all the participants signed written informed consent.

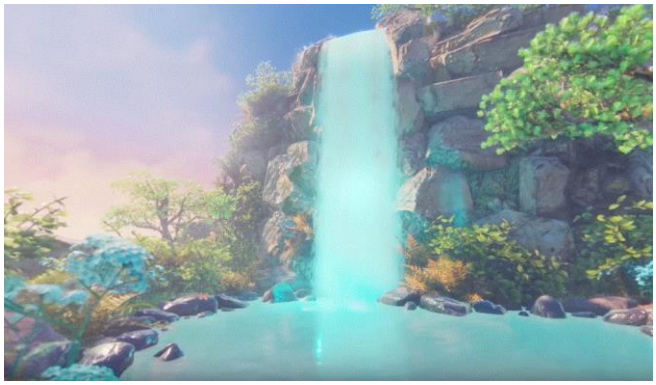

*Figure 7: The VE*[8]. *A screenshot from the virtual environment*

Subsequently, every participant was presented with the two versions of the VE (the same VE with body scan or respiration control narrative), presented in a randomized order. Participants were said they could interrupt the experience in the case of negative sensations. Before any exposure and after each exposure, the participants were asked to fill in questionnaires.

Considering the instructions given in the two conditions, in the breathing condition the exercise involved breathing control processes to slow down breath frequencies, making every breathing act lasting 4 seconds ("*Breathe in through your nose and out through your nose or mouth. Feel your stomach expand on an inhale and relax and let go as you exhale*"… "*slowly inspire.. hold your breath... And breathe out... Hold your breath*"). The body scan condition instead required to bring attention to body sensations, trying to feel tensions and unpleasant feelings and to let them go ("*Now slowly bring your attention down to your feet. Begin observing sensations in your feet*"..."*bring your attention to the contact with the*

[8] The original version of the virtual environment used in the study was developed by Prosoma Digital Therapeutics.

*floor*”).

After completing the two exercises and after the completion of the post-exposure questionnaires, participants were asked:

1) to imagine describing their VR experience to a relevant person,

2) to describe past effective relaxing experiences, comparing them with the VR experience.

*Measures*

Before the VE experience, participants filled in a questionnaire including demographic variables, previous experiences with VR technology, and relaxation techniques. Participants were also asked to complete an ad hoc question on perceived relaxation level as a baseline (relaxation level on a line of 10 cm length Visual Analogue Scale (VAS)), and the Self-Assessment Manikin (SAM) for the emotional baseline. The latter is a three-item visual scale (valence, intensity/arousal, dominance) commonly used to quantify properties of the felt overall emotional state on 1 to 5 scales of images (Bradley & Lang, 1994).

After each exposure to the VE experience, participants filled in a questionnaire on the relaxation techniques used in the narratives, which included 1) VAS scales of 10 cm length, asking the levels of relaxation experienced, easiness of exercise, the effectiveness of the exercise, and pleasantness, 2) SAM again, 3) a brief description of the concept of being present inside a VE, and a VAS of 10 cm length to assess the sense of presence. After both exposures, participants were asked to state which technique they would like to repeat.

*Statistical Analysis*

We measured the frequencies for the explicit self-report preference on which exercises participants would repeat. We performed ANOVA repeated measures for relaxation levels and for SAM item, which were assessed in three-time points (before any intervention and after both the exercises), and then paired t-test to assess significant differences.

We used paired t-test to determine differences between the two exercises for the remaining variables.

*3.4.2 Results*

Analyses explored participants' responses to the VE versions and, when possible, compared them with baseline values. No cybersickness responses were observed in any participant. Overall, 10 participants would have repeated the Body Scan exercise, while 3 did not express a preference for a specific technique and 3 preferred the breathing exercise.

*Relaxation*

The first analysis was a Repeated Measures ANOVA that compared relaxation level before any stimulation and after the exposure to the two versions of the Waterfall VE. A significant difference emerged from the paired t-test performed between relaxation levels after the two techniques, showing that patients felt more relaxed after the exposure to the Body Scan version (M=8.4, SD=1.78) compared to the Breathing one (M=7.3, SD=2.6) (Table 1). Both the scores were significantly higher than the relaxation level registered at baseline ((M=4.1, SD=2.08): $F(2,28)=22.803$, $p=.001$, $\eta^2=.62$).

The second analysis compared the two versions of the Waterfall VE in terms of patients' attitudes/evaluation, namely easiness of exercise; effectiveness; pleasantness; and sense of presence. Paired t-tests did not obtain significant results. Table 10 shows the mean results, revealing how each version of the VE obtained positive scores according to patients' perception.

*Emotional state*

SAM evaluations (the emotional state in terms of valence, arousal, dominance) were analyzed with Repeated Measures ANOVAs. Dominance did not yield significant results. Instead, patients experienced a more pleasant state (i.e. valence) after the exposure to the Body Scan version of the Waterfall VE (M=8.2, SD=1.23), than after the Breathing version of it (M=7.9, SD=1.52), even if the difference did not reach statistical significance ($t(15)=-2.07$, $p=.055$). Both the scores were higher than the pleasantness level registered at baseline ((M=6.6, SD=1.7): $F(2,28)=10.720$, $p=.001$, $\eta^2=.43$). Also, patients experienced less intense activation (arousal) after the exposure to the Body Scan version of the Waterfall VE (M=2.3,

SD=2.05), rather than after the Breathing version of it (M=2.8, SD=2.33), though the difference was not significant ($t(15)=1.86$, p=.08). Both the scores were lower than arousal intensity registered at baseline ((M=4.4, SD=1.99): $F(2,28)=5.654$, $p=.009$, $\eta^2=.28$). For both the exercises, valence, and arousal scores were statistically different compared to the baseline levels. Specifically, valence in the Breathing version was more positive compared to the baseline ($t(15)=-3.27$, $p=.005$), as well as in the Body scan version ($t(15)=-3.65$,$p=.002$). Arousal scores also decreased from the baseline after the Breathing version ($t(15)=2.16$, $p=.04$) and the Body scan one ($t(15)=2.89$, $p=.01$).

Table 10: *Comparison between the two exercises*

| *Psychological features of the experience with the VEs* | *Mean, s.d.* | |
|---|---|---|
| | ***Breathing*** | ***BodyScan*** |
| Relaxation* (t= -3.432) | 7.38, 2.6 | 8.44, 1.7 |
| Easiness of exercise | 8.52, 1.1 | 8.65, 1.1 |
| Effectiveness | 7.73, 2.2 | 8.39, 1.1 |
| Pleasantness | 8.17, 2 | 8.64, 1.2 |
| Sense of Presence | 5.79, 3.2 | 6.09, 3.1 |

* $p < .05$

*Subjective experiences and preferences*

The most recurrent themes among personal reports were organized according to the perceptual/sensorial features of the experiences that were emphasized and liked the most. The dimensions that came out from the qualitative reports were the importance of bodily sensations, the pleasantness of warm features, and the prominence of auditive modality over the other perceptual modalities to reach relaxation.

Overall, participants mentioned perceptual features mostly focused on body sensations and

awareness and reported those sensations to be effective and relaxing.

In particular, participants described relaxing sensations related to body perception and muscles, rather than related to focusing on breathing and cognitive processes or thoughts. Consistently with subjective experiences, the body-focused exercise was preferred. A participant reported that she felt to be in contact with her body "*I felt the body and a progressive sensation of calm and relaxation*", while others told "*I felt the sensation of being heavy and relaxed starting from the hands*" or "*muscles started to relax*". Interestingly, a participant said that she felt an improvement of awareness and an enhanced perception of pain inside her body "*I felt the feet and pain of the back*" and that being in touch with the body made her feel calm.

The second feature was the warm temperature, a characteristic that was reported to be pleasant and that was used to describe stimuli across sensorial modalities (related to voice, colours, body temperature). For example, some participants reported that "*the voice was warm*" and "*the voice was calm and warm*", while for what concerns colours it has been told "*I remember warm and vivid colours*" and "*the warm sun*". Considering body sensations *"I felt hot thought the body"* and "*my body became warm*".

Lastly, the perceptual modality that was perceived as inducing relaxation the most was hearing (music, water sounds, and guiding voice), rather than sight. Interestingly, most of the participants closed their eyes during the sessions and almost all the subjects commented on the voice "*the voice was calm.. Strong and warm*", "*I remember.. The sound of water*", *"the voice was more important than the VR itself "*. Notably, in two cases, participants did not like the tone of the voice or the fact that it was slow, pointing out that individual differences do occur in preferences for the relaxing features.

### *3.4.3 Discussion*

Results showed that the Waterfall VE versions were effective in providing relaxation to participants. Specifically, relax level was significantly higher after exposure to the VEs than

at the baseline. The same efficacy was observed for emotional valence and arousal levels. Secondarily, a comparison between the two versions of the VEs showed that also the difference between the two was significant, specifically the Body scan narrative brought more relaxation in the users. Noteworthy, most of the participants reported a preference for the body scan exercise.

These first results provide important information: first, they corroborate literature findings on VR being able to relax users, breast cancer patients specifically; secondly, they show that the audio narratives based on specific approaches to relaxation are not just secondary add-ons to the VEs, on the contrary, they guarantee specific experiences to the users.

It is interesting to note that the versions of the Waterfall VE differed in participants' perception regarding experienced relaxation and emotional valence/arousal, which is the subjective self-report of physical sensations, while no differences emerged regarding participants' opinions on the VE's properties (easiness of the exercise, effectiveness, pleasantness), as well as regarding the sense of being present in the VR. Indeed, the VE was the same across conditions, but the overall experience was not, because the different narratives involved the users in diverse ways.

Notable, 12 participants already tried yoga practices. Even if we cannot assess quantitative differences in our experiment, we can speculate firstly that cancer patients may feel the necessity of being engaged in relaxing practices, secondly, that body scan might have been more effective than breathing exercise, as most of the subjects already had a certain degree of expertise with the latter, being somehow more familiar to reach relaxation through breathing control.

In the end, despite both versions of the Waterfall VE obtained positive scores, the Body scan narrative was associated with more relaxation and more positive and less arousing emotional activation. These preliminary results point out that employing body-focused exercises for cancer patients might yield a major efficacy compared to the breathing exercises, that have been extensively used until now in relaxing VR.

An important objective for future research is to understand whether such a difference should be attributed to the superiority of body scan or body-focused techniques over respiration techniques (or, to the body scan techniques being more adequate to be included in VR experiences than others) or, on the contrary, to specific characteristics of the clinical sample involved in the present research. Indeed, breast cancer patients' stress and anxiety struggles are strictly connected to distorted experiences relating to the body and the body image. When cancer is diagnosed, one's physique could start to be perceived as an extraneous object, a source of disease and threat, so that patients may feel disconnected from their own body (Rosenblatt, 2006). Despite breast cancer is one of the most treatable cancers at the medical level (Chang et al., 2018), psychotherapy and psychological support should address its damaging effects on patients' body image, which directly affect patients' and survivors' intimacy, self-image, and self-esteem. For patients with health issues, tailoring relaxation techniques on specific needs has indeed resulted to be effective (Wang et al., 2019).

Immersive technologies, such as VR to provide relaxation, could be more effective in addressing patients' experience specifically, following the user-centered approaches to technology design for healthcare.

Body scan techniques, compared to respiration control, might be more effective in helping patients to regain contact and control over their own body and the interoceptive/proprioceptive inputs, this way providing an aware embodied relaxing experience.

Future studies should involve patients with different illness experiences, to understand whether some relaxation techniques' effectiveness in VR is specifically connected to the subjective experience of specific pathological conditions and treatment side effects.

Finally, as regards qualitative and subjective experiences, reports described perceptual features mostly focused on body sensations and awareness ("*I felt the sensation of being heavy and relaxed starting from the hands*", "*muscles started to relax", "I felt the feet and pain of the back"*), the most frequent being warm temperature, related to voice, colors, body

temperature (*"the voice was warm"*, *"I remember warm and vivid colors"*, *"I felt hot thought the body"*). The modality patients perceived as inducing relaxation the most was hearing (music, water sounds, and guiding voice), rather than sight ("*the voice was calm... Strong and warm*", "*I remember... The sound of water*", *"the voice was more important than the VR itself"*).

Overall, these results stressed the importance of bodily sensations to reach a good state of calmness and relaxation and highlighted the importance of the tone of the guiding voice.

The fact that the voice was more commented than the VE and the visual features (some participants closed their eyes), might be due to the fact that the visual scene was not interactive, and that the technique was delivered mainly by the voice. However, at the beginning of the exercises, the guiding voice asked participants to look and pay attention to the scenario. Furthermore, the virtual scenario might have played an unrecognized role, making the participants feel present in the waterfall VE and allowing them to be more focused on the exercises.

*Limitations*

The results should be interpreted in light of some limitations.

First, the study included only breast cancer patients' survivors, which means that the results might not be generalized to other cancer types or other stages of the breast cancer disease.

Second, the within-subjects design did not allow for a comparison with a control group of healthy subjects or other patients.

Thirdly, the sample size was small.

Moreover, the employed exercises were a brief version of techniques that might require more time to be effective. We could not conclude on the possible effects of the length of the exercises.

Lastly, the exercises did not imply interaction with the VE or with virtual stimuli, thus we cannot rule out the possibility of a moderation effect of interaction with VR contents on patients' preference and perceived efficacy.

## 4. Empirical contribution: the incorporation of olfactory cues in virtual environments for personalized relaxation[9]

*Overview*

The following contribution is a proposal on the implementation of the use of olfaction in the field of personalized relaxation in the general and clinical population (i.e., clinical samples with anxiety symptoms).

The studies previously presented in the dissertation, aimed at adding empirical knowledge to the users' preferences on relaxation, relaxation contents, and the efficacy of some specific relaxation exercises.

Since peculiar scents can trigger emotional reactions or autobiographical memories, a further step in the direction of tailoring digital interventions for relaxation might be the inclusion of scents in digital environments.

This inclusion might yield greater efficacy and more possibilities of personalization.

*The sense of smell*

The following contribution proposes three applications of the sense of smell inside relaxation interventions in VR. Indeed, given its features, the sense of olfaction can enhance relaxation and emotion regulation.

As Patrick Süskind (1985) describes in his novel *Perfume: The Story of a Murderer*: "*Odors have a power of persuasion stronger than that of words, appearances, emotions, or will. The persuasive power of an odor cannot be fended off, it enters us like breath into our lungs, it fills us up, imbues us totally. There is no remedy for it.*"

The smell is phylogenetically the most ancient sense. It has a unique and closer relationship with emotions and homeostasis than other sensory modalities (Delplanque, Coppin, & Sander, 2017). It is related to energy balance, reward, disgust, and aversive signals (Morris,

[9] Adapted from Pizzoli, S.F.M., & Monzani, D., Mazzocco, K., Maggioni, E., Pravettoni, G. *The power of odor persuasion: A perspective paper on the incorporation of olfactory cues in virtual environments for personalized relaxation.* Under review.

2017; Riera et al., 2017). Indeed, the olfactory system is also wired to automatic learned responses (aversive or appetitive) (Choi et al., 2011). It can directly stimulate the amygdala, side-stepping a thalamic relay, rendering the perception of smells powerfully linked with emotions (Van Hartevelt & Kringelbach, 2012; Warrenburg, 2005). Evidence shows that the more prominent characteristic of olfactory perception is the emotional and affective experience (Khan et al., 2007; Krusemark, Novak, Gitelman, & Li, 2013; Yeshurun & Sobel, 2010). For instance, consider the positive emotions that arise when smelling the scents of one's childhood, such as freshly baked cookies or the laundry detergent used by loved ones. Fragrances can also influence cognition, social behaviour (for a review, see (Sowndhararajan & Kim, 2016)), mood, and quality of life (Cramer, Friedman, & Amick, 2010; Hong et al., 2015; Smeets et al., 2009). Aromas have a modulating effect on psychophysiological activity and arousal (Moss, Cook, Wesnes, & Duckett, 2003). The potential mechanisms through which odor yields these effects include modulated attentional processes (Maggioni, Cobden, Dmitrenko, & Obrist, 2018; Rinaldi, Maggioni, Olivero, Maravita, & Girelli, 2018) memory tasks (Shanahan, Gjorgieva, Paller, Kahnt, & Gottfried, 2018) and judgment and decision making (Bonini, Graffeo, Hadjichristidis, & Perrotta, 2015; Bonini et al., 2011).

The sense of smell can also prompt recollection of remote autobiographical memories (Chu & Downes, 2000; Herz & Schooler, 2002; Willander & Larsson, 2007), while other sensorial modalities cannot. This effect is referred to as the “Proust phenomenon”, from an often-quoted episode from Proust’s life, in which the author describes a vivid unintended re-evocation of a childhood experience triggered by the taste of tea and madeleine. Interestingly, the flooding back described by Proust displays some essential features of odors recall, involving old memories, affective experiences, and involuntary and automatic recall. Common examples may be the perfume of a beloved one immediately activating past affective memories or an unpleasant smell of foods that had made us feel sick triggering automatically an aversive sensation (Boesveldt, Frasnelli, Gordon, & Lundström, 2010). Notably, compared to other re-evoking cues (e.g., words and pictures), olfactory stimuli can

evoke autobiographical memories with more emotional and vivid experiences (Herz, Eliassen, Beland, & Souza, 2004; Herz & Schooler, 2002; Willander & Larsson, 2006). Furthermore, the higher the familiarity of an odor, the higher its perceived pleasantness (Bensafi et al., 2003; Engen & Ross, 1973).

*Olfaction in the field of relaxation and emotion regulation*

Given its emotional valence, the use of smell in clinical practice might give rise to newer possibilities to enhance patient involvement and foster the efficacy of clinical techniques. This might be especially true for relaxation exercises, one of the most common tools in psychological clinical settings. Traditionally, relaxation procedures ask clients to leverage imagery of calming scenes of past pleasant experiences to modulate psychophysiological arousal. Mindful attention to the breath and progressive muscle relaxation are also often incorporated into clinical practice (Smith, 1999). Overall, these techniques encompass both top-down and bottom-up processes. While the former involves cognitive control, attention shifting, sustained attention, and memory recall, the latter requires senses awareness and psychophysiological modulation, lowering arousal and muscle contraction.

Given the emotion- and memory-related features of olfaction, its utilization in relaxation might have several benefits, both in the case of imaginary relaxing scenes and in the case of autobiographical memories. Olfaction stimulation might also stress bottom-up processes, one of the main targets of several relaxation strategies. Indeed, behavioural studies showed that olfactory stimuli can evoke automatic rather than conscious reactions (Atsumi & Tonosaki, 2007; Mark et al., 2018). Some chemicals can induce autonomic activations that are related to mating, eating aversive reactions, and disgust (Boesveldt et al., 2010; Sarafoleanu, Mella, Georgescu, & Perederco, 2009; Walla, 2008).

However, unlike other sensorial modalities, it is hard to manipulate, stimulate or evoke olfactory sensations with imagination (Auffarth, 2013). For this reason, despite its promising results for relaxation, olfaction is rarely employed in clinical settings (for an earlier review see Martin (1996)). Among the main examples of its use in clinical practices, King observed

a reduction of anxiety symptoms in subjects exposed to pleasant smells combined with a relaxation technique (King, 1983). Similarly, pleasant scents induced a perceived state of relaxation and a perceived reduction of depressive symptoms (Schiffman & Siebert, 1991; Schiffman, 1992). Exposure to natural pleasant scents is also associated with a reduction of heart rate frequencies, blood pressure, and negative affect (Dong & Jacob, 2016). Furthermore, Abramowitz and Lichtenberg (2009, 2010) developed the so-called 'hypnotherapeutic olfactory conditioning', a procedure in which patients undergoing hypnosis learn to associate pleasant scents with a sense of security and personal control. The authors found preliminary positive results for the application of this technique to the treatment of patients with Post Traumatic Stress Disorder (PTSD).

Currently, emerging technologies in the field of VR might make it possible to apply olfaction stimulation in VR relaxing interventions and give rise to new clinical perspectives.

*VR and olfaction: smelling relaxation.*

VR for relaxation can bring the benefits of classical relaxation techniques derived from yoga, meditation, and muscle relaxation into VEs. VR per se may also solve difficulties that arise in applying classical relaxation techniques. For example, VR might help people with low mental imagery to perform imagery relaxation tasks. Additionally, VR can decrease the cognitive burden of relaxation techniques that require the contemporary following instructions and using mental imagery. Typically, VR interventions take advantage of 2-3 sensorial modalities (Freeman et al., 2017), focusing on the involvement of visual and auditory stimuli and, less frequently, tactile elements. VR for relaxation usually employs natural landscapes or other natural stimuli, which are considered to have intrinsic relaxing properties and narratives that directly derive or combine instructions from the classical practices.

However, recent developments in the field of eHealth (Camerini, Camerini, & Schulz, 2013; Spanakis et al., 2016; Vergani et al., 2019) and VR interventions go in the direction of contents personalization based on relevant personal and autobiographical

content (Alcañiz et al., 2007; Botella et al., 2010). We propose that involving the sense of smell with olfactory stimuli within VEs might enhance both the effectiveness of relaxing intervention and the implementation of more personalized VEs.

Indeed, the higher emotional impact provided by scents throughout the re-activation of autobiographical memories might give some valuable advantages in VR settings. First, smells can enhance a higher sense of presence (Baus & Bouchard, 2017; Jones & Dawkins, 2018; Munyan III, Neer, Beidel, & Jentsch, 2016), even if there are still inconclusive results. For instance, while Dinh et al (1999) found a significant effect of smells on memory for but not on the sense of presence, Baus and Bouchard found an increased sense of presence when unpleasant odors were put inside VR (2017). However, this effect was not reported for pleasant scents which, however, can enhance the sense of perceived reality (Baus, Bouchard, & Nolet, 2019).

Scents can augment affective activation and provide an additional sensorial channel stimulation besides classical VR modalities (e.g., visual, audio, tactile). In this way, the sensorial experience might become more similar to one of the real worlds, where we use all our senses.

The second advantage of using scents inside VR is leveraging the emotional engagement that can make relaxation more effective. Scents can provide sensorial experiences and perceptions that are not entirely mediated by cortical elaboration and that can activate almost automatically emotion-related contents or experiences. Lastly, because olfactory cues are strongly associated with autobiographical memories, scents may support the personalization of VR settings to clients' past experiences.

*Olfaction relaxation meets VR: possible applications.*

Although olfactory inputs have received less attention than other sensorial features of VR interventions (Chen, 2006; Matsukura, Yoneda, & Ishida, 2013), the idea of using scents inside the VR is not new (Aiken & Berry, 2015; Baus & Bouchard, 2014; Chen, 2006; Obrist, Gatti, Maggioni, Vi, & Velasco, 2017; Obrist, Tuch, & Hornbaek, 2014). A review by Baus

and Bouchard (Baus & Bouchard, 2010) provided a comprehensive overview of features of scents and possible applications within VR settings. Starting from the first VR prototype by Heilig, The Sensorama, which made use of all the senses, nowadays smells have been proposed as valuable perceptual elements in treating PTSD through presence enhancement (Aiken & Berry, 2015; Rizzo et al., 2010). Other studies deepened the possibility to deliver smells in interaction with multimedia content (Amores & Maes, 2017; Dobbelstein, Herrdum, & Rukzio, 2017; Maggioni et al., 2018) to improve cognitive performances in different activities, such as attention during car-driving.

Here we propose three non-mutually exclusive applications of olfactory stimuli within VR aimed at relaxation and dropping arousal stressing states. We will expand on mechanisms involved in such hypothetical applications (Table 11) and describe interventions' features (Table 12). We divided the proposed applications into three different interventions, namely (1) classical relaxation, (2) personalized relaxation, and (3) personalized exposure therapy. All the interventions involve the olfactory sensorial channel to modulate and lower arousal. Notably, the interventions differ from each other for the link with personal contents, the specific aim of the relaxation, and how scents should be delivered within the relaxation sessions.

For each intervention, we trace some common features that can be used to describe, characterize, distinguish, and compare the three. Regarding the processes involved in the interventions (Table 11), we considered six different dimensions that can be used to describe and compare the three types of interventions: 1) perceptual involvement; 2) arousal modulation; 3) emotional link; 4) personalization based on autobiographical experiences; 5) personalization based on user preferences; 6) desensitization/extinction. Perceptual involvement refers to the fact that the interventions try to achieve user relaxation through sensorial engagement, while arousal modulation and emotional link refer to the modality by which the state would be achieved, respectively by lowering physiological activity or activating positive emotions. The two dimensions related to the personalization of contents

point out the fact that the building of the three interventions can benefit from user-centered approaches. While the former focuses on personal preferences, the latter aims at using or recreating relevant autobiographical cues. Finally, desensitization/extinction refers to the therapeutically psychophysiological process implying the reduction of the association between perceived threatening stimuli and anxiety response.

We also describe differences and commonalities between the interventions regarding the population to target (users: general vs. clinical population), the choice of olfactory stimuli (scents with intrinsic relaxing properties vs. user-centered or autobiographical relaxing scents), and their modulation (scent modulation: gradual vs. stable), as well as the scenario type (relaxing, tailored relaxing, tailored exposure) and the awareness of the olfactory perception (the consciousness of sensorial perception: conscious perception vs subconscious perception) (Table 12).

Table 11*: Psychological and physiological processes targeted by the three proposed interventions.*

| | ***Interventions*** | | |
|---|---|---|---|
| | ***Relaxation*** | ***Personalized relaxation*** | ***Personalized exposure therapy*** |
| *Perceptual involvement* | ● | ● | ● |
| *Arousal modulation* | ● | ● | ● |
| *Emotional link* | ● | ● | ● |

| | | | |
|---|---|---|---|
| *Personalization based on autobiographical experiences* | | ● | ● |
| *Personalization based on users' preferences* | | ● | ● |
| *Desensitization/extinction* | | | ● |

Table 12*: Technical features of the interventions.*

| | ***Interventions*** | | |
|---|---|---|---|
| | ***Relaxation*** | ***Personalized relaxation*** | ***Personalized exposure therapy*** |
| ***Users*** | *General population*<br><br>*Clinical population* | *General population*<br><br>*Clinical population* | *Clinical population* |
| ***Scents*** | *Intrinsic relaxing properties* | *User-centered or autobiographical relaxing scents* | *Intrinsic relaxing properties*<br><br>*User-centered or autobiographical relaxing scents* |

| | | | |
|---|---|---|---|
| ***Scent modulation*** | *Gradual or stable* | *Gradual or stable* | *Gradual* |
| ***Scenario*** | *Relaxing scenarios* | *Tailored relaxing scenarios* | *Tailored exposure scenarios* |
| ***The consciousness of sensorial perception*** | *Conscious perception* | *Conscious or subconscious perception* | *Conscious perception* |

*Classical relaxation*

The first intervention deals with the employment of scents with intrinsic relaxation properties, such as linalool scents ( Atsumi & Tonosaki, 2007; Harada, Kashiwadani, Kanmura, & Kuwaki, 2018; Sowndhararajan & Kim, 2016). From this perspective, scents could be used as relaxing stimuli per se, like natural visual scenarios usually employed in relaxation interventions. Advantages in using scents in this kind of relaxation may be represented by an enhanced emotional experience as well as an augmented sense of presence. For example, a study employing 3D images and fragrances used scents for targeting relaxation (Kawai & Noro, 1996). To the best of our knowledge, only one recent study involving both touch and smell used lavender scents to improve relaxation in a general population sample (Serrano, Baños, & Botella, 2016). The authors did not find significant results for relaxation. Since they used a simple delivery procedure (i.e., a ceramic diffuser), they advanced that other (simpler or more complicated) delivery procedures might yield different results. We hypothesize that a more controllable procedure, for example delivering scents synchronized with the instructions of the relaxation technique, might increase the effectiveness of the relaxation procedure.

*Personalized relaxation*

The “Personalized Relaxation” approach goes in the direction of personalizing the VR content. It is an attempt to collect and use autobiographical relevant scents to give users personalized experiences and emotionally charged perceptions inside the VE. Such intervention is congruent with the personalized VR approach (Pizzoli et al., 2019), aiming at building user-centered VEs, filled with multimodal stimuli derived from users' autobiographical elements. To collect scent categories, a qualitative approach similar to the one used by Obrist and colleagues (2014) should be used. It consists of gathering personal autobiographical smells (i.e. “smells stories”) and extracting personalized scents libraries. Such an approach would be the operationalization of what has been referred to as the Proust phenomenon: in a personalized smell-evoking setting it would be possible to activate autobiographical memories, even when the user does not deliberatively intend to re-experience them. Thus, the use of autobiographical scents may have the advantage to access remote memories as well as the benefit of lowering the cognitive load required to re-evoke memories and experiences (Keller, 2011, 2014; Seigneuric, Durand, Jiang, Baudouin, & Schaal, 2010). Thus, this will render easily to follow narratives and instructions and perform relaxation exercises. Furthermore, since the familiarity of an odor is positively related to its perceived pleasantness (Bensafi et al., 2003; Engen & Ross, 1973), using familiar scents, after having assessed subjective preferences for specific smells, would then increase the pleasantness of users’ experience and would enhance positive sensations. User preferences should also be assessed by evaluating the more preferred specific sensorial features and intensity of scents.

*Personalized exposure therapy*

The third intervention type is the most prominently focused on the therapeutical application since it is conceptualized to target clinical symptoms. While the first two techniques take inspiration from relaxing practices and can be applied to reach a state of relaxation both on laypeople and on persons struggling with clinical symptoms, this third intervention type uses techniques specifically applied in specific psychiatric conditions, such

as phobias and PTSD. Indeed, this last intervention takes advantage of exposure procedures, classical conditioning extinction, and desensitization by way of combining user exposure to stressful visual-auditory stimuli with exposure to pleasant and presumably safe smells. It would be an attempt to gradually manipulate scents through the variation of delivery parameters like time, intensity, and pressure and consequently to achieve emotional desensitization during virtual reality exposure therapies (VRET). Being an ancient way to perceive the world and sending automatic survivorship-related messages to the brain, olfaction might provide the possibility to send relaxing or safe signals to the brain, while the subject is exposed to a virtual scene associated with trauma or high stress. In this perspective, scents will be used to reach the extinction of the association between traumatic triggers and arousal. Remarkable, pleasant scents can decrease arousal levels (Alaoui-Ismaïli et al., 1997; Knasko, 1992), an effect strongly targeted by desensitization practices.

Desensitization practices can be useful when a traumatic trigger induces excessive arousal reactions associated with a traumatic trigger. In the field of VR, some examples of the application of scents combined with the treatment of fear and anxiety associated with a perceived threat are mainly present for PTSD disease. However, our application differs from the procedure already used for PTSD patients (Aiken & Berry, 2015; Gerardi, Rothbaum, Ressler, Heekin, & Rizzo, 2008; Morina et al., 2017; Rizzo & Shilling, 2018) or exposure therapy (Munyan III et al., 2016). Specifically, while in these procedures scents are used to re-evoke traumatic sensations in a realistic way or to enhance the sense of presence of the patients, here we propose to employ smell as a therapeutic means. Being emotionally charged stimuli bounded with an evolutionary sense of survivorship, relaxing and positive scents may support clients' desensitization to the traumatic scene. Such an olfaction extinction phenomenon has been already studied in adult mice, showing neuroanatomical changes and reverse in freezing behaviours, following extinction training with odors (Morrison, Dias, & Ressler, 2015). This study is of note, considering olfactory cues may be associated with traumatic experiences in both humans and mice. Moreover, olfactory

receptive fields among humans maintain plasticity and the consequent capacity for adaptation in response to environmental stimuli across the lifespan (Morrison et al., 2015). For such interventions, both intrinsic relaxing scents and personalized odors would be useful. Notably, in the already cited studies by Abramowitz and Lichtenberg (2009, 2010), who found promising results on pairing hypnosis and scents to treat patients with PTSD and to overcome phobias and prevent panic attacks, scents were chosen according to patient's prior experiences. Indeed, patients were asked to choose scents that were already associated with calming memories and imagery.

Albeit exploiting olfaction to reach extinction between arousal and traumatic triggers would be extremely difficult in clinical settings, new VR tools may render this possibility feasible in the next years within VRET, expanding possible therapeutically applications of the VR. Indeed, the extinction of the association between a perceived threat and excessive arousal can be beneficial for psychiatric conditions (Kong, Monje, Hirsch, & Pollak, 2014), where the difficulty of extinguishing learned fear might occur (i.e. phobias, generalized anxiety disorders, panic disorder (DSM-5, 2013)).

*Current obstacles and developing tools*

Despite promising application, it is worthy of note that olfaction stimuli and devices devoted to scents administration present several difficulties, both technical (Kaye, 2004) and related to the nature of the stimulus (Auffarth, 2013). First, prolonged exposure to odorants may provoke both peripheral and central adaptation, leading to a decrease of sensorial sensitivity (Dalton, 2000; Poellinger et al., 2001). Olfaction can also adapt itself according to arousal levels and emotions (Krusemark et al., 2013; Pollatos et al., 2007), thus there is a problem linked to the sensorial level of stimulations and real-time receptor adaptation. Adaptation would be a problem specifically for known odors, as the sensitivity to new smells is largely intact (Köster & de Wijk, 1991). Furthermore, a single olfactory percept embraces multiple odorants. This could represent an issue when trying to reproduce autobiographical scents since the remembered percept can be composed of a multitude of different odorants.

Secondly, individual differences in scents perception that are linked to biological (age, sex) (Good, Kopala, & Doherty, 2006; Pause, Sojka, Krauel, Fehm-Wolfsdorf, & Ferstl, 1996) and cultural factors may take place (Ghinea & Ademoye, 2011). Lastly, even if emotional valence and autobiographical relevance can be valuable advantages, they can also constitute limits, as it may be difficult to establish a priori affective reactions to scents, from a qualitative and a quantitative point of view. Unconscious and automatic reactions should be explicitly explored, to avoid negative or aversive associations. Subliminal perceptions should be carefully assessed particularly in the case of personalized exposure, where the desensitization process depends directly on associating sensations of safeness with stressful elements. User-specific responses to scents (e.g., perceived valence) need to be considered in clinical settings to ensure inadvertently aversive scents are not used with clients, as this could reinforce the very associations that the procedure is aiming to weaken. To overcome these limits, specific guidelines for the development of the construction of VR intervention as a meaningful therapeutical tool can be followed (Birckhead et al., 2019). They suggested starting from accurate pilot studies, to assess the specific needs of the population of interest and its specific psychiatric symptoms. Olfaction threshold should also be assessed since it might depend on biological and temperamental factors (age, trait or state anxiety, sex) as well as the condition to target (relaxation or specific desensitization). Psychophysiological correlates should also be continuously monitored, both prior and during the intervention, to allow for the adjustment of the stimulation depending on the moment-by-moment psychophysiological state.

To realize the proposals of the present work, two main practical solutions can be traced. One approach is to diffuse scents inside the whole room users are in by using a kit with smelling palettes. Another approach is to use small devices connected to the VR headset. This approach can deliver scents directly close to the user's head or in the real environment with a high reliable scent-delivery device, synchronized with the VR settings and user actions. The first solution however has some limitations, as it does not account for the habituation

phenomena and the room scent saturation, while the second more advanced scent-delivery device with a highly controllable scent delivery can avoid these limitations and provide personalization through the selection of scent preferences. Noteworthy, to date, some private companies are already trying to develop such tools, offering new possibilities both to conduct preliminary studies on user-preferred autobiographical scents and to perform precise pilot experiments assessing odors and their combination and quantity. Scents palettes bring the possibility to combine several olfactory stimuli, ranging from organic smells to artificial ones, and to make a refined combination of different olfactory elements, embracing specific users' needs.

Besides stimuli features, methods to deliver olfactory stimuli have been dramatically improved in the last few decades, starting from the first rather basic odors delivery methods (i.e. squeezing bottles containing scents or the first olfactometers) (Walla, 2008) to ad hoc and self-made computerized tools (Johnson & Sobel, 2007; Lorig, Elmes, Zald, & Pardo, 1999; Lundström, Gordon, Alden, Boesveldt, & Albrecht, 2010). Currently, an overview of the state of art on scent-delivery devices as well as an evaluation of a scent-delivery portable device can be found in Risso and colleagues. (Risso, Covarrubias Rodriguez, Bordegoni, & Gallace, 2018). Other technology, as OWidgets (Maggioni, Cobden, & Obrist, 2019), allows for the integration of scents with the VEs and can direct the user attention using delivery outcomes with predefined spatial location or triggered by the scene in the VE or movement/action of the users. Technologies such as this can facilitate user-tailored and dynamic experiences inside VE with the application of olfactory stimuli.

To date, all these methodologies have been scarcely employed in clinical practice because of objective difficulties in delivering them to the general customer. Up to now, technological applications dealing with the properties of scents have been used in the field of human-machine interaction, aiming at improving user efficiency (Dmitrenko, Maggioni, Vi, & Obrist, 2017; Maggioni et al., 2018; Seigneuric et al., 2010). Up to now, the clinical application of these methodologies has been limited to date to treat addiction and related

disorders (Bordnick et al., 2008; Marissen, Franken, Blanken, van den Brink, & Hendriks, 2007).

To summarize, the sense of smell can be a powerful way to access the inner emotional world when presented in VEs. Current obstacles linked to sensorial stimulation threshold and odor delivery are starting to be addressed by new technological applications, bringing newer opportunities for VR experiences, and opening possibilities not only for the entertainment and video-games industry but also for clinical interventions tailored according to patient's features.

## 5. Conclusions

Effective relaxation interventions can be beneficial in general and for persons with medical conditions, such as cancer patients.

The personalization of relaxation experiences comprises the assessment of the individual differences, which can account for different preferences, and the evaluation of the specific features of the digital stimuli to be included in the interventions.

The present project collected evidence on some elements which should be considered before the construction of tailored digital interventions for relaxation.

The study presented in this dissertation aimed at evaluating separate elements that can be used to personalize digital interventions for relaxation.

For this aim, the user-centered approach was applied to measure users' preferences, while a quantitative approach was utilized to examine the efficacy of the narratives and the exercises to be put inside the interventions.

It is important to assess the users' preferences on the specific features of the tools employed in relaxation. Indeed, the simple evaluation of a pre-constituted digital intervention would not inform on the users' preferences regarding the single elements of the intervention (the scenario, the sounds, the narrative) and on which dimensions can be varied to give an effective personalization.

From the studies included in the present dissertation, heterogeneous preferences among the general population and cancer patients emerged.

These results might suggest the dimensions on which a variability among preferences can be found and that consequently might be used for designing the tailored interventions.

Specifically, the first group of studies evaluated, in the general population, the profile of preferences for relaxation habits, the possible association between individual differences and habits, the possibility of using relevant autobiographical stimuli as digital stimuli inside VR, and the efficacy of three different relaxation techniques that might be put inside the VR.

Firstly (*Relaxation preferences and individual differences in response to stressors*), the information collected pointed out that some individual differences, such as the strategies used to react to stressors (coping styles) and gender, might be associated with relaxation habits and relaxation preferences. Future studies might evaluate a possible causal role of the coping styles on relaxation habits, as well as the possibility of predicting relaxation preferences starting from coping styles. Furthermore, the habits that were preferred the most were based on the need for sensorial relaxation. The importance of the bodily sensorial features emerged also in other studies of the present work. Thus, tailored digital interventions should grant the possibility of targeting bodily sensations with dedicated narratives or virtual experiences.

Secondly (*The personal Safe Place*), considering autobiographical stimuli, the following consideration can be drawn from the results.

The type of the environment of the safe place (setting: from close to open spaced dimensions), the presence of other persons (sharing: from solitude to the presence of people), and the type of activity that the subjects were doing in their safe places (engagement: from passive and resting to active), might be considered dimensions to be varied according to users' preferences. Future interventions might indeed plan to include the possibility of tailoring pre-constituted digital environments according to these three dimensions.

Thirdly (*A comparison of remote relaxation experience: a randomized controlled study*), as regards the efficacy of different relaxation exercises which can be digitally and remotely delivered, relevant results emerged.

All three techniques (natural sounds, square breathing, and body scan) resulted to be effective in relaxing users. Thus, all three might be employed in future interventions that will use narratives to relax the users.

The employed techniques were delivered only as audio clips; thus, they were tested without confounding factors which usually occur in digital interventions (the scenarios, the background sounds...). Consequently, the features that rendered the exercises effective, are

strictly related to the type of exercise and the auditive features of the clips. Interestingly, some participants commented on the voice of the instructor.

The body scan, which resulted to be effective, might be employed in future digital and remote interventions for relaxation and it might be included to offer the possibility of experiencing relaxing body sensations, which is an element that emerged in the two previous studies. Furthermore, future studies might evaluate the features of the guiding voice which are associated with different preferences or with enhanced efficacy. It might be also interesting to test a combination of the three techniques or longer versions of the exercises.

The second group of studies evaluated some features of relaxing experiences, to inform the construction of personalized interventions focused on cancer patients' needs and preferences.

Firstly (*User-centered design on hospitalized cancer patients*), hospitalized cancer patients' specific needs and preferences on relaxation and the digital scenarios were assessed. It seems that hospitalized cancer patients think that VR for relaxation might be a useful tool during hospitalization. Moreover, different preferences emerged for what concerns the characteristics of the digital scenarios that might be employed. This points to the need for a careful assessment of patient's preferences on digital scenarios. Additionally, the are some dimensions of the digital environments that might be considered as relevant dimensions to be changed according to patients' preferences (the colours, reality of the scenes, and the presence of avatars).

The second and the third study (*The Waterfall environment, Tailoring relaxing experience on breast cancer patients: a pilot study*) of the second section utilized the same VE, to test the relaxation properties of a virtual relaxation experience. While the first study assessed the relaxation properties of the scenario per se, the second tested two versions of the scenario, filled with two distinct narratives with different relaxation exercises. This second study also examined the qualitative experience with the exercises and was conducted on breast cancer

patients. The collected data pointed out again the importance of bodily sensations and of the voice used for the recording of the techniques.

The main findings from the six studies might inform the construction of tailored digital relaxing interventions.

The key points that emerged might constitute the premises for the construction of a library of stimuli and features. This library might be a priori built to give users the possibility of choosing their preferred features and of tailoring their own interventions.

To summarize, the following main points might be taken as hints for the construction of a library of stimuli and features, which can be personalized according to the specific needs and preferences of the users.

*Synthesis of the results*

To systematize the elements of the relaxation interventions that should be considered in future tailored digital interventions, the results from the reported studies were organized into techniques and stimuli features.

The present summary of findings put together all the dimensions and features on which users' expressed preferences.

Techniques*:*

- *Body-focused experiences*: one of the most replicated results, in both the general population and cancer patients, was the importance of bodily sensations. In particular the sensations of feeling the muscles heavy and relaxed. In line with these preferences, the body scan exercise resulted to be effective and appreciated by participants.

  Such a result is consistent with the evidence that the muscle relaxation therapy is effective and feasible in the treatment of anxiety symptoms, specifically of panic disorder and generalized anxiety disorder (Conrad & Roth, 2007), and also with the fact that body-focused relaxation exercises (such as progressive muscle relaxation) yield several benefits to cancer patients (Kapogiannis et al., 2018; De Paolis et al.,

2019 ). Thus, future digital interventions should consider the importance of targeting the perception of the body and of guiding the users in muscle relaxation.

Notably, in the present studies, the featured relaxation techniques were one-session guided interventions. Therefore, this evidence might be used to support the use of a single session exercise. Future studies might assess users' preferences for other body-focused techniques, as well as for prolonged training, which might include body-focused exercises, mixed with other approaches.

- *The degree of autonomy and activity*: participants expressed different preferences regarding the degree of involvement they would like to have during relaxation practices and exercises. Future personalized digital interventions might present exercises with different levels of involvements required from the users (from active to passive). Moreover, some exercises might be fully guided by the narratives, while others might leave a major degree of autonomy to users, for example leaving a dedicated time to free thoughts and imagination.

  Coping styles, gender, and previous relaxation habits might offer insight into the likelihood of users' preferences on this dimension.

<u>Stimuli:</u>

- *Water*: water has been reported as one of the main preferred elements in the users' centered studies. It has been recounted in autobiographical reports and it has been described as a pleasant element of the virtual scenarios. Participants commented on the presence of water, its colours and sounds, and, in the case of relaxation habits or memories, its temperature. The inclusion of this stimulus can be recommended in relaxation interventions and, for digital interventions, it might be reproduced in a visual or auditive way.
- *Temperature:* temperature, in particular warm sensations, were appreciated by several participants. The experience of warmth was reported in the form of sensorial stimulation in the case of users' preferences on relaxation habits (warm places, hot

showers), but it was also referred to as the warmness of colours and voices included in the digital interventions.

In the case of digital scenarios, it might be useful to include the possibility of tailoring the colours and some elements of the scenarios (such as sunset, fire) to reproduce the sensation of heat.

- *Auditive features*: the auditive stimuli (voices, sounds, and music) should be carefully built for future interventions since auditory features were described as one of the elements which absorb the attention the most during relaxation. Indeed, auditive features were important for relaxation habits and autobiographical reports, and in the case of the tone of the guiding voice and natural sounds included in the digital scenarios.

  While assessing auditory features to be included, future studies should consider elements such as the speed and the tone of the guiding voice, as well as the preferences for natural sounds (for example water sounds) and their combination with the guiding voice.

- *Light and colours*: the levels of illumination and the vividity of colours were commented on by many participants. While a clear preference for certain types of colours and illuminations did not appear, the fact that many participants commented on these aspects suggests that these features may represent a relevant element in relaxing experiences. Notably, in the hospitalized cancer sample, some participants reported disliking red features of the digital scenarios, because of the association between blood and red. Future interventions might give the possibility of varying the levels of light in digital scenes, according to users' preferences.

- *Avatar and Interaction:* a fair degree of variability has been found in preferences for what concerns the presence of relevant others and the interaction with them. Some participants preferred relaxing experiences lived in solitude, while others favoured more social experiences. Relevant figures to interact with were both persons and

animals. Thus, users of relaxing tailored digital interventions might be provided with the possibility of choosing the level of social interaction and the type of avatars to be inserted. In the case of relaxing experiences, animals seem to be a valuable type of avatar to be included.

- *Olfaction:* when possible, scents might be included in digital relaxation interventions, because of their direct link with inner emotional states.

  Relaxation interventions might not use only scents which are already known to be intrinsically relaxing, but they might also include scents linked with autobiographical memories and thus with powerful emotional meanings.

To conclude, a further step in the direction of the construction of personalized digital interventions for relaxation might be the creation of a digital tool, with the form of a library, from which users might choose to vary some features of pre-constitute intervention, to meet their specific needs and preferences.

The techniques and stimuli here summarized might provide an initial guide for the construction of such a library.

If the personalization of relaxation techniques increases their efficacy, leading to an improvement in individuals' well-being, the use of VR will contribute to the amelioration of care by acting on two main levels: on the individual level, tailoring the intervention on the individual's specific needs and preferences; on the health system level, increasing the number of patients having access to such interventions, when human resources are limited.

## References


Abramowitz, E. G., & Lichtenberg, P. (2009). Hypnotherapeutic olfactory conditioning (HOC): Case studies of needle phobia, panic disorder, and combat-induced PTSD. *International Journal of Clinical and Experimental Hypnosis*, *57*(2), 184–197. https://doi.org/10.1080/00207140802665450

Abramowitz, E. G., & Lichtenberg, P. (2010). A new hypnotic technique for treating combat-related posttraumatic stress disorder: A prospective open study. *International Journal of Clinical and Experimental Hypnosis*, *58*(3), 316–328. https://doi.org/10.1080/00207141003760926

Aiken, M. P., & Berry, M. J. (2015). Posttraumatic stress disorder: possibilities for olfaction and virtual reality exposure therapy. *Virtual Reality*, *19*(2), 95–109. https://doi.org/10.1007/s10055-015-0260-x

Alaoui-Ismaïli, O., Robin, O., Rada, H., Dittmar, A., & Vernet-Maury, E. (1997). Basic emotions evoked by odorants: Comparison between autonomic responses and self-evaluation. *Physiology and Behavior*, *62*(4), 713–720. https://doi.org/10.1016/S0031-9384(97)90016-0

Alcañiz, M., Botella, C., Rey, B., Baños, R., Lozano, J. A., de la Vega, N. L., … Hospitaler, A. (2007). *EMMA: An Adaptive Display for Virtual Therapy*. https://doi.org/10.1007/978-3-540-73216-7_29

Alexander, C. N., Langer, E. J., Newman, R. I., Chandler, H. M., & et al. (1989). Transcendental Meditation, mindfulness, and longevity: An experimental study with the elderly. *Journal of Personality and Social Psychology*, *57*(6), 950–964. https://doi.org/10.1037//0022-3514.57.6.950

Alvarsson, J. J., Wiens, S., & Nilsson, M. E. (2010). Stress recovery during exposure to nature sound and environmental noise. *International Journal of Environmental Research and Public Health*, *7*(3), 1036–1046. https://doi.org/10.3390/ijerph7031036

Amores, J., & Maes, P. (2017). Essence: : Olfactory Interfaces for Unconscious Influence of

Mood and Cognitive Performance. *Proceedings of the 2017 CHI Conference on Human Factors in Computing Systems - CHI '17*, 28–34. https://doi.org/10.1145/3025453.3026004

Anderson, A. P., Mayer, M. D., Fellows, A. M., Cowan, D. R., Hegel, M. T., & Buckey, J. C. (2017). Relaxation with Immersive Natural Scenes Presented Using Virtual Reality. *Aerospace Medicine and Human Performance*, *88*(6), 520–526. https://doi.org/10.3357/AMHP.4747.2017

Andersson, G. (2016). Internet-Delivered Psychological Treatments. *Annual Review of Clinical Psychology*, *12*(1), 157–179. https://doi.org/10.1146/annurev-clinpsy-021815-093006

Andersson, G., Cuijpers, P., Carlbring, P., Riper, H., & Hedman, E. (2014). Guided Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: A systematic review and meta-analysis. *World Psychiatry*, *13*(3), 288–295. https://doi.org/10.1002/wps.20151

Annerstedt, M., Jönsson, P., Wallergård, M., Johansson, G., Karlson, B., Grahn, P., … Währborg, P. (2013). Inducing physiological stress recovery with sounds of nature in a virtual reality forest — Results from a pilot study. *Physiology & Behavior*, *118*, 240–250. https://doi.org/10.1016/j.physbeh.2013.05.023

Arcos-Carmona, I. M., Castro-Sánchez, A. M., Matarán-Peñarrocha, G. A., Gutiérrez-Rubio, A. B., Ramos-González, E., & Moreno-Lorenzo, C. (2011). Efectos de un programa de ejercicios aeróbicos y técnicas de relajación sobre el estado de ansiedad, calidad del sueño, depresión y calidad de vida en pacientes con fibromialgia: ensayo clínico aleatorizado. *Medicina Clínica*, *137*(9), 398–401. https://doi.org/10.1016/j.medcli.2010.09.045

Arnaboldi, P., Riva, S., Crico, C., & Pravettoni, G. (2017). A systematic literature review exploring the prevalence of post-traumatic stress disorder and the role played by stress and traumatic stress in breast cancer diagnosis and trajectory. *Breast Cancer: Targets*

*and Therapy*, *Volume 9*, 473–485. https://doi.org/10.2147/BCTT.S111101

Aspinwall, L. G., & Taylor, S. E. (1992). Modeling cognitive adaptation: A longitudinal investigation of the impact of individual differences and coping on college adjustment and performance. *Journal of Personality and Social Psychology*, *63*(6), 989–1003. https://doi.org/10.1037//0022-3514.63.6.989

Astin, J. A., Beckner, W., Soeken, K., Hochberg, M. C., & Berman, B. (2002). Psychological interventions for rheumatoid arthritis: A meta-analysis of randomized controlled trials. *Arthritis Care and Research*, *47*(3), 291–302. https://doi.org/10.1002/art.10416

Atsumi, T., & Tonosaki, K. (2007). Smelling lavender and rosemary increases free radical scavenging activity and decreases cortisol level in saliva. *Psychiatry Research*, *150*(1), 89–96. https://doi.org/10.1016/j.psychres.2005.12.012

Auffarth, B. (2013). Understanding smell—The olfactory stimulus problem. *Neuroscience & Biobehavioral Reviews*, *37*(8), 1667–1679. https://doi.org/10.1016/J.NEUBIOREV.2013.06.009

Bai, Y. M., Lin, C. C., Lin, C. Y., Chen, J. Y., Chue, C. M., & Chou, P. (2004). Survey of stress reactions among health care workers involved with the SARS outbreak. *Psychiatric Services*, *55*(9), 1055–1057. https://doi.org/10.1176/appi.ps.55.9.1055

Bani Mohammad, E., & Ahmad, M. (2018). Virtual reality as a distraction technique for pain and anxiety among patients with breast cancer: A randomized control trial. *Palliative and Supportive Care*. https://doi.org/10.1017/S1478951518000639

Baños, R., Botella, C., Quero, S., García-Palacios, A., & Alcañiz, M. (2011). Engaging Media for Mental Health Applications: the EMMA project. *Studies in Health Technology and Informatics*, *163*, 44–50. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/21335756

Baños, R. M., Etchemendy, E., Castilla, D., García-Palacios, A., Quero, S., & Botella, C. (2012). Positive mood induction procedures for virtual environments designed for elderly people. *Interacting with Computers*, *24*(3), 131–138.

https://doi.org/10.1016/j.intcom.2012.04.002

Baños, Rosa M, Botella, C., Guerrero, B., Liaño, V., Alcañiz, M., & Rey, B. (2005). The third pole of the sense of presence: Comparing virtual and imagery spaces. *PsychNology Journal*, *3*(1), 90–100. https://doi.org/10.1089/cpb.2008.0056

Baños, Rosa M, Espinoza, M., García-Palacios, A., Cervera, J. M., Esquerdo, G., Barrajón, E., & Botella, C. (2013). A positive psychological intervention using virtual reality for patients with advanced cancer in a hospital setting: a pilot study to assess feasibility. *Supportive Care in Cancer : Official Journal of the Multinational Association of Supportive Care in Cancer*, *21*(1), 263–270. https://doi.org/10.1007/s00520-012-1520-x

Barkan, T., Hoerger, M., Gallegos, A. M., Turiano, N. A., Duberstein, P. R., & Moynihan, J. A. (2016). Personality Predicts Utilization of Mindfulness-Based Stress Reduction during and Post-Intervention in a Community Sample of Older Adults. *Journal of Alternative and Complementary Medicine*, *22*(5), 390–395. https://doi.org/10.1089/acm.2015.0177

Baumeister, H., Reichler, L., Munzinger, M., & Lin, J. (2014, October 1). The impact of guidance on Internet-based mental health interventions - A systematic review. *Internet Interventions*, Vol. 1, pp. 205–215. https://doi.org/10.1016/j.invent.2014.08.003

Baus, O., & Bouchard, S. (2014). Moving from Virtual Reality Exposure-Based Therapy to Augmented Reality Exposure-Based Therapy: A Review. *Frontiers in Human Neuroscience*, *8*(January 2010). https://doi.org/10.3389/fnhum.2014.00112

Baus, O., & Bouchard, S. (2017). Exposure to an unpleasant odour increases the sense of Presence in virtual reality. *Virtual Reality*, *21*(2), 59–74. https://doi.org/10.1007/s10055-016-0299-3

Baus, O., Bouchard, S., & Nolet, K. (2019). Exposure to a pleasant odour may increase the sense of reality, but not the sense of presence or realism. *Behaviour and Information Technology*, *38*(12), 1369–1378. https://doi.org/10.1080/0144929X.2019.1590458

Bensafi, M., Rouby, C., Farget, V., Bertrand, B., Vigouroux, M., & Holley, A. (2003). Perceptual, affective, and cognitive judgments of odors: pleasantness and handedness effects. *Brain and Cognition*, *51*(3), 270–275. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12727181

Benson, H, & Proctor, W. (2010). *Relaxation Revolution: : The science and genetics of mind body healing* (SIMON & SCHUSTER, Ed.).

Benson, Herbert, Beary, J. F., & Carol, M. P. (1974). The Relaxation Response. *Psychiatry*, *37*(1), 37–46. https://doi.org/10.1080/00332747.1974.11023785

Bernstein, D. A., & Borkovec, T. D. (1973). *Progressive relaxation training : a manual for the helping professions*. Research Press.

Beutel, M. E., Klein, E. M., Brähler, E., Reiner, I., Jünger, C., Michal, M., … Tibubos, A. N. (2017). Loneliness in the general population: Prevalence, determinants and relations to mental health. *BMC Psychiatry*, *17*(1), 97. https://doi.org/10.1186/s12888-017-1262-x

Bhasin, M. K., Dusek, J. A., Chang, B. H., Joseph, M. G., Denninger, J. W., Fricchione, G. L., … Libermann, T. A. (2013). Relaxation Response Induces Temporal Transcriptome Changes in Energy Metabolism, Insulin Secretion and Inflammatory Pathways. *PLoS ONE*, *8*(5). https://doi.org/10.1371/journal.pone.0062817

Birckhead, B., Khalil, C., Liu, X., Conovitz, S., Rizzo, A., Danovitch, I., … Spiegel, B. (2019). Recommendations for Methodology of Virtual Reality Clinical Trials in Health Care by an International Working Group: Iterative Study. *JMIR Mental Health*, *6*(1), e11973. https://doi.org/10.2196/11973

Bishop, S. R., Lau, M., Shapiro, S., Carlson, L., Anderson, N. D., Carmody, J., … Devins, G. (2004). Mindfulness: A proposed operational definition. *Clinical Psychology: Science and Practice*. https://doi.org/10.1093/clipsy/bph077

Bodnar, A., Corbett, R., & Nekrasovski, D. (2004). AROMA: Ambient awaReness through Olfaction in a Messaging Application Does Olfactory Notification Make “Scents”?

*Proceedings of the 6th International Conference on Multimodal Interfaces - ICMI '04*, 183. https://doi.org/10.1145/1027933.1027965

Boesveldt, S., Frasnelli, J., Gordon, A. R., & Lundström, J. N. (2010). The fish is bad: Negative food odors elicit faster and more accurate reactions than other odors. *Biological Psychology*, *84*(2), 313–317. https://doi.org/10.1016/j.biopsycho.2010.03.006

Bonini, N., Graffeo, M., Hadjichristidis, C., & Perrotta, V. (2015). The effects of incidental scents in the evaluation of environmental goods: The role of congruity. *PsyCh Journal*, *4*(2), 66–73. https://doi.org/10.1002/pchj.76

Bonini, N., Hadjichristidis, C., Mazzocco, K., Demattè, M. L., Zampini, M., Sbarbati, A., & Magon, S. (2011). Pecunia olet: The role of incidental disgust in the ultimatum game. *Emotion*, *11*(4), 965–969. https://doi.org/10.1037/a0022820

Bordnick, P. S., Traylor, A., Copp, H. L., Graap, K. M., Carter, B., Ferrer, M., & Walton, A. P. (2008). Assessing reactivity to virtual reality alcohol based cues. *Addictive Behaviors*, *33*(6), 743–756. https://doi.org/10.1016/j.addbeh.2007.12.010

Botella, C., García-Palacios, A., Guillen, V., Baños, R. M., Quero, S., & Alcaniz, M. (2010). An adaptive display for the treatment of diverse trauma PTSD victims. *Cyberpsychology, Behavior and Social Networking*, *13*(1), 67–71. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20528295

Braboszcz, C., Rael Cahn, B., Levy, J., Fernandez, M., & Delorme, A. (2017). Increased gamma brainwave amplitude compared to control in three different meditation traditions. *PLoS ONE*, *12*(1), 1–27. https://doi.org/10.1371/journal.pone.0170647

Bradley, M M, & Lang, P. J. (1994). Measuring emotion: the Self-Assessment Manikin and the Semantic Differential. *Journal of Behavior Therapy and Experimental Psychiatry*, *25*, 49–59. https://doi.org/10.1016/0005-7916(94)90063-9

Brandmeyer, T., Delorme, A., & Wahbeh, H. (2019). The neuroscience of meditation: classification, phenomenology, correlates, and mechanisms. In *Progress in Brain*

*Research* (Vol. 244, pp. 1–29). https://doi.org/10.1016/bs.pbr.2018.10.020

Brooks, S. K., Webster, R. K., Smith, L. E., Woodland, L., Wessely, S., Greenberg, N., & Rubin, G. J. (2020, March 14). The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *The Lancet*, Vol. 395, pp. 912–920. https://doi.org/10.1016/S0140-6736(20)30460-8

Brown, K. W., & Ryan, R. M. (2003). The Benefits of Being Present: Mindfulness and Its Role in Psychological Well-Being. *Journal of Personality and Social Psychology*. https://doi.org/10.1037/0022-3514.84.4.822

Camerini, L., Camerini, A.-L., & Schulz, P. J. (2013). Do participation and personalization matter? A model-driven evaluation of an Internet-based patient education intervention for fibromyalgia patients. *Patient Education and Counseling*, *92*(2), 229–234. https://doi.org/10.1016/j.pec.2013.04.007

Carlson, L. E., Zelinski, E. L., Toivonen, K. I., Sundstrom, L., Jobin, C. T., Damaskos, P., & Zebrack, B. (2019). Prevalence of psychosocial distress in cancer patients across 55 North American cancer centers. *Journal of Psychosocial Oncology*, *37*(1), 5–21. https://doi.org/10.1080/07347332.2018.1521490

Carver, C. S., Scheier, M. F., & Weintraub, J. K. (1989b). Assessing coping strategies: A theoretically based approach. *Journal of Personality and Social Psychology*, *56*(2), 267–283. https://doi.org/10.1037//0022-3514.56.2.267

Chang, B.-H., Dusek, J. A., Zaki, J., Lazar, S. W., Deykin, A., Stefano, G. B., … Benson, H. (2006). *Association between oxygen consumption and nitric oxide production during therelaxation response Association between oxygen consumption and nitric oxide production during the relaxation response*. Retrieved from https://www.researchgate.net/publication/284544426

Chang, L., Weiner, L. S., Hartman, S. J., Horvath, S., Jeste, D., Mischel, P. S., & Kado, D. M. (2018). Breast cancer treatment and its effects on aging. *Journal of Geriatric Oncology*.

Charalambous, A., Giannakopoulou, M., Bozas, E., Marcou, Y., Kitsios, P., & Paikousis, L. (2016). Guided imagery and progressive muscle relaxation as a cluster of symptoms management intervention in patients receiving chemotherapy: A randomized control trial. *PLoS ONE*, *11*(6). https://doi.org/10.1371/journal.pone.0156911

Chen, Y. (2006). Olfactory Display: Development and Application in Virtual Reality Therapy. *16th International Conference on Artificial Reality and Telexistence--Workshops (ICAT'06)*, 580–584. https://doi.org/10.1109/ICAT.2006.95

Chen, Y. F., Huang, X. Y., Chien, C. H., & Cheng, J. F. (2017). The Effectiveness of Diaphragmatic Breathing Relaxation Training for Reducing Anxiety. *Perspectives in Psychiatric Care*, *53*(4), 329–336. https://doi.org/10.1111/ppc.12184

Chirico, A., Lucidi, F., De Laurentiis, M., Milanese, C., Napoli, A., & Giordano, A. (2016a). Virtual Reality in Health System: Beyond Entertainment. A Mini-Review on the Efficacy of VR During Cancer Treatment; Virtual Reality in Health System: Beyond Entertainment. A Mini-Review on the Efficacy of VR During Cancer Treatment. *J. Cell. Physiol*, *231*, 275–287. https://doi.org/10.1002/jcp.25117

Choi, G. B., Stettler, D. D., Kallman, B. R., Bhaskar, S. T., Fleischmann, A., & Axel, R. (2011). Driving opposing behaviors with ensembles of piriform neurons. *Cell*, *146*(6), 1004–1015. https://doi.org/10.1016/j.cell.2011.07.041

Chu, S., & Downes, J. J. (2000). Odour-evoked Autobiographical Memories: Psychological Investigations of Proustian Phenomena. *Chemical Senses*, *25*(1), 111–116. https://doi.org/10.1093/chemse/25.1.111

Cohen, S., Janicki-Deverts, D., & Miller, G. E. (2007, October 10). Psychological stress and disease. *Journal of the American Medical Association*, Vol. 298, pp. 1685–1687. https://doi.org/10.1001/jama.298.14.1685

Conklin, C. A., & Tiffany, S. T. (2002). Applying extinction research and theory to cue-exposure addiction treatments. *Addiction (Abingdon, England)*, *97*(2), 155–167. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11860387

Conklin, Q. A., King, B. G., Zanesco, A. P., Lin, J., Hamidi, A. B., Pokorny, J. J., … Saron, C. D. (2018). Insight meditation and telomere biology: The effects of intensive retreat and the moderating role of personality. *Brain, Behavior, and Immunity*, *70*, 233–245. https://doi.org/10.1016/j.bbi.2018.03.003

Conrad, A. & Roth, W. . (2007). Muscle Relaxation for Anxiety Disorder : It works but how?. *The Journal of Anxiety Disorder*, 243-264. Retrieved from https://www.sciencedirect.com/science/article/pii/S0887618506001174

Cordova, M. J., Riba, M. B., & Spiegel, D. (2017). Post-traumatic stress disorder and cancer. The Lancet Psychiatry, 4(4), 330-338.

Courtin, E., & Knapp, M. (2017, May 1). Social isolation, loneliness and health in old age: a scoping review. *Health and Social Care in the Community*, Vol. 25, pp. 799–812. https://doi.org/10.1111/hsc.12311

Cox, B. J., Endler, N. S., Swinson, R. P., & Norton, G. R. (1992). Situations and specific coping strategies associated with clinical and nonclinical panic attacks. *Behaviour Research and Therapy*, *30*(1), 67–69. https://doi.org/10.1016/0005-7967(92)90099-3

Cramer, C. K., Friedman, J. H., & Amick, M. M. (2010). Olfaction and apathy in Parkinson's disease. *Parkinsonism & Related Disorders*, *16*(2), 124–126. https://doi.org/10.1016/j.parkreldis.2009.09.004

Crawford, D. W., Godbey, G., & Crouter, A. C. (1986). The stability of leisure preferences. *Journal of Leisure Research*, *18*(2), 96–115. https://doi.org/10.1080/00222216.1986.11969649

Dalton, P. (2000). Psychophysical and behavioral characteristics of olfactory adaptation. *Chemical Senses*, *25*(4), 487–492. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10944515

Dascal, J., Reid, M., Ishak, W. W., Spiegel, B., Recacho, J., Rosen, B., & Danovitch, I. (2017). Virtual reality and medical inpatients: A systematic review of randomized, controlled trials. *Innovations in Clinical Neuroscience*, Vol. 14, pp. 14–21. Retrieved

from http://www.ncbi.nlm.nih.gov/pubmed/28386517

De Paolis, G., Naccarato, A., Cibelli, F., D'Alete, A., Mastroianni, C., Surdo, L., … Magnani, C. (2019, February 1). The effectiveness of progressive muscle relaxation and interactive guided imagery as a pain-reducing intervention in advanced cancer patients: A multicentre randomised controlled non-pharmacological trial. *Complementary Therapies in Clinical Practice*, Vol. 34, pp. 280–287. https://doi.org/10.1016/j.ctcp.2018.12.014

de Rooij, I. J. M., van de Port, I. G. L., & Meijer, J.-W. G. (2016). Effect of Virtual Reality Training on Balance and Gait Ability in Patients With Stroke: Systematic Review and Meta-Analysis. *Physical Therapy*, *96*(12), 1905–1918. https://doi.org/10.2522/ptj.20160054

Del Barrio, V. (2016). Diagnostic and statistical manual of mental disorders. In *The Curated Reference Collection in Neuroscience and Biobehavioral Psychology*. https://doi.org/10.1016/B978-0-12-809324-5.05530-9

Delplanque, S., Coppin, G., & Sander, D. (2017). Odor and Emotion. In *Handbook of Odor* (pp. 101–102).

Dinh, H. Q., Walker, N., Hodges, L. F., Song, C., & Kobayashi, A. (1999). Evaluating the importance of multi-sensory input on memory and the sense of presence in virtual environments. *Proceedings - Virtual Reality Annual International Symposium*, 222–228. Retrieved from https://jhu.pure.elsevier.com/en/publications/evaluating-the-importance-of-multi-sensory-input-on-memory-and-th-3

Ditto, B., Eclache, M., & Goldman, N. (2006). Short-term autonomic and cardiovascular effects of mindfulness body scan meditation. *Annals of Behavioral Medicine*, *32*(3), 227–234. https://doi.org/10.1207/s15324796abm3203_9

Dmitrenko, D., Maggioni, E., Vi, C. T., & Obrist, M. (2017). What Did I Sniff? *Proceedings of the 9th International Conference on Automotive User Interfaces and Interactive Vehicular Applications - AutomotiveUI '17*, *17*, 154–163.

https://doi.org/10.1145/3122986.3122998

Dobbelstein, D., Herrdum, S., & Rukzio, E. (2017). inScent: a wearable olfactory display as an amplification for mobile notifications. *Proceedings of the 2017 ACM International Symposium on Wearable Computers - ISWC '17*, 130–137. https://doi.org/10.1145/3123021.3123035

Dockx, K., Bekkers, E. M., Van den Bergh, V., Ginis, P., Rochester, L., Hausdorff, J. M., … Nieuwboer, A. (2016). Virtual reality for rehabilitation in Parkinson's disease. *Cochrane Database of Systematic Reviews*, *12*, CD010760. https://doi.org/10.1002/14651858.CD010760.pub2

Donald, J. N., & Atkins, P. W. B. (2016). Mindfulness and Coping with Stress: Do Levels of Perceived Stress Matter? *Mindfulness*, *7*(6), 1423–1436. https://doi.org/10.1007/s12671-016-0584-y

Dorrepaal, K. L., Aaronson, N. K., & Van Dam, F. S. A. M. (1989). Pain experience and pain management among hospitalized cancer patients. A clinical study. *Cancer*, *63*(3), 593–598. https://doi.org/10.1002/1097-0142(19890201)63:3<593::AID-CNCR2820630332>3.0.CO;2-5

Dusek, Jeffery A., & Benson, H. (2009). Mind-body medicine: a model of the comparative clinical impact of the acute stress and relaxation responses. *Minnesota Medicine*, *92*(5), 47–50. Retrieved from /pmc/articles/PMC2724877/?report=abstract

Dusek, Jeffrey A., Otu, H. H., Wohlhueter, A. L., Bhasin, M., Zerbini, L. F., Joseph, M. G., … Libermann, T. A. (2008). Genomic counter-stress changes induced by the relaxation response. *PLoS ONE*, *3*(7). https://doi.org/10.1371/journal.pone.0002576

Eisenberg, S. A., Shen, B. J., Schwarz, E. R., & Mallon, S. (2012). Avoidant coping moderates the association between anxiety and patient-rated physical functioning in heart failure patients. *Journal of Behavioral Medicine*, *35*(3), 253–261. https://doi.org/10.1007/s10865-011-9358-0

Endler, N. S., & Parker, J. D. (1990). Multidimensional assessment of coping: A critical

evaluation. *Journal of Personality and Social Psychology*, *58*(5), 844–854. https://doi.org/10.1037//0022-3514.58.5.844

Engen, T., & Ross, B. M. (1973). Long-term memory of odors with and without verbal descriptions. *Journal of Experimental Psychology*, *100*(2), 221–227. https://doi.org/10.1037/h0035492

Eppley, K. R., Abrams, A. I., & Shear, J. (1989). Differential effects of relaxation techniques on trait anxiety: A meta-analysis. *Journal of Clinical Psychology*, *45*(6), 957–974. https://doi.org/10.1002/1097-4679(198911)45:6<957::AID-JCLP2270450622>3.0.CO;2-Q

Esch, T., Fricchione, G. L., & Stefano, G. B. (2003, February 1). The therapeutic use of the relaxation response in stress-related diseases. *Medical Science Monitor*, Vol. 9. MSI Medical Science International Publishing.

Espinoza, M., Baños, R. M., García-Palacios, A., Cervera, J. M., Esquerdo, G., Barrajón, E., & Botella, C. (2012). Promotion of emotional wellbeing in oncology inpatients using VR. *Studies in Health Technology and Informatics*, *181*, 53–57. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/22954828

Eysenbach, G., & CONSORT-EHEALTH Group. (2011, December 31). CONSORT-EHEALTH: improving and standardizing evaluation reports of Web-based and mobile health interventions. *Journal of Medical Internet Research*, Vol. 13, p. e126. https://doi.org/10.2196/jmir.1923

Felix, M. M. dos S., Ferreira, M. B. G., da Cruz, L. F., & Barbosa, M. H. (2017). Relaxation Therapy with Guided Imagery for Postoperative Pain Management: An Integrative Review. *Pain Management Nursing*. https://doi.org/10.1016/j.pmn.2017.10.014

Fredborg, B., Clark, J., & Smith, S. D. (2017). An Examination of Personality Traits Associated with Autonomous Sensory Meridian Response (ASMR). *Frontiers in Psychology*, *8*(FEB), 247. https://doi.org/10.3389/fpsyg.2017.00247

Freeman, D., Reeve, S., Robinson, A., Ehlers, A., Clark, D., Spanlang, B., & Slater, M.

(2017). Virtual reality in the assessment, understanding, and treatment of mental health disorders. *Psychological Medicine*, *47*(14), 2393–2400. https://doi.org/10.1017/S003329171700040X

Gaitan-Sierra, C., & Hyland, M. E. (2014). Mood enhancement in health-promoting non-aerobic exercise: The role of non-specific mechanisms. *Journal of Health Psychology*, *19*(7), 918–930. https://doi.org/10.1177/1359105313482163

Galvin, J. A., Benson, H., Deckro, G. R., Fricchione, G. L., & Dusek, J. A. (2006). The relaxation response: Reducing stress and improving cognition in healthy aging adults. *Complementary Therapies in Clinical Practice*, *12*(3), 186–191. https://doi.org/10.1016/j.ctcp.2006.02.004

Garrett, B., Taverner, T., Masinde, W., Gromala, D., Shaw, C., & Negraeff, M. (2014). A rapid evidence assessment of immersive virtual reality as an adjunct therapy in acute pain management in clinical practice. *The Clinical Journal of Pain*, *30*(12), 1089–1098. https://doi.org/10.1097/AJP.0000000000000064

Gerardi, M., Rothbaum, B. O., Ressler, K., Heekin, M., & Rizzo, A. (2008). Virtual reality exposure therapy using a virtual Iraq: case report. *Journal of Traumatic Stress*, *21*(2), 209–213. https://doi.org/10.1002/jts.20331

Gerge, A. (2018). REVISITING THE SAFE PLACE:Method and Regulatory Aspects in Psychotherapy when Easing Allostatic Overload in Traumatized Patients. *International Journal of Clinical and Experimental Hypnosis*, *66*(2), 147–173. https://doi.org/10.1080/00207144.2018.1421356

Gershon, J., Zimand, E., Lemos, R., Rothbaum, B. O., & Hodges, L. (2003). Use of Virtual Reality as a Distractor for Painful Procedures in a Patient with Pediatric Cancer: A Case Study. *CyberPsychology & Behavior*, *6*(6), 657–661. https://doi.org/10.1089/109493103322725450

Gershon, J., Zimand, E., Pickering, M., Rothbaum, B. O., & Hodges, L. (2004). A pilot and feasibility study of virtual reality as a distraction for children with cancer. *Journal of*

*the American Academy of Child and Adolescent Psychiatry*, *43*(10), 1243–1249. https://doi.org/10.1097/01.chi.0000135621.23145.05

Ghinea, G., & Ademoye, O. A. (2011). Olfaction-enhanced multimedia: perspectives and challenges. *Multimedia Tools and Applications*, *55*(3), 601–626. https://doi.org/10.1007/s11042-010-0581-4

Gibson, J. (2019). Mindfulness, Interoception, and the Body: A Contemporary Perspective. *Frontiers in Psychology*, *10*. https://doi.org/10.3389/fpsyg.2019.02012

Goldberg, S. B., Tucker, R. P., Greene, P. A., Davidson, R. J., Wampold, B. E., Kearney, D. J., & Simpson, T. L. (2018). Mindfulness-based interventions for psychiatric disorders: A systematic review and meta-analysis. *Clinical Psychology Review*, *59*(1), 52–60. https://doi.org/10.1016/j.cpr.2017.10.011

Good, K. P., Kopala, L., & Doherty, P. (2006). Sex Differences and Olfactory Function. In W. J. Brewer, D. Castle, & C. Pantelis (Eds.), *Olfaction and the Brain* (pp. 183–202). https://doi.org/10.1017/CBO9780511543623.012

Gorini, A., Pallavicini, F., Algeri, D., Repetto, C., Gaggioli, A., & Riva, G. (2010). Virtual reality in the treatment of generalized anxiety disorders. *Studies in Health Technology and Informatics*, *154*, 39–43. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20543266

Griffin, A. M., Butow, P. N., Coates, A. S., Childs, A. M., Ellis, P. M., Dunn, S. M., & Tattersall, M. H. (1996). On the receiving end. V: Patient perceptions of the side effects of cancer chemotherapy in 1993. *Annals of Oncology : Official Journal of the European Society for Medical Oncology*, *7*(2), 189–195. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8777177

Gruzelier, J. H. (2002). A review of the impact of hypnosis, relaxation, guided imagery and individual differences on aspects of immunity and health. *Stress*, *5*(2), 147–163. https://doi.org/10.1080/10253890290027877

Guze, S. B. (1995). Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-

IV). *American Journal of Psychiatry*. https://doi.org/10.1176/ajp.152.8.1228

Harada, H., Kashiwadani, H., Kanmura, Y., & Kuwaki, T. (2018). Linalool Odor-Induced Anxiolytic Effects in Mice. *Frontiers in Behavioral Neuroscience*, *12*(October), 1–8. https://doi.org/10.3389/fnbeh.2018.00241

Heber, E., Ebert, D. D., Lehr, D., Cuijpers, P., Berking, M., Nobis, S., & Riper, H. (2017, February 1). The benefit of web- and computer-based interventions for stress: A systematic review and meta-analysis. *Journal of Medical Internet Research*, Vol. 19. https://doi.org/10.2196/jmir.5774

Heyse, J., De Jonge, T., Vega, M. T., De Backere, F., & De Turck, F. (2019, June). A personalized virtual reality experience for relaxation therapy. In 2019 Eleventh International Conference on Quality of Multimedia Experience (QoMEX) (pp. 1-3). Ieee.

Hegde, S. V., Adhikari, P., Kotian, S., Pinto, V. J., D'Souza, S., & D'Souza, V. (2011). Effect of 3-month yoga on oxidative stress in type 2 diabetes with or without complications: A controlled clinical trial. *Diabetes Care*, *34*(10), 2208–2210. https://doi.org/10.2337/dc10-2430

Herz, R. S., Eliassen, J., Beland, S., & Souza, T. (2004). Neuroimaging evidence for the emotional potency of odor-evoked memory. *Neuropsychologia*, *42*(3), 371–378. https://doi.org/10.1016/j.neuropsychologia.2003.08.009

Herz, R. S., & Schooler, J. W. (2002). A naturalistic study of autobiographical memories evoked by olfactory and visual cues: Testing the Proustian hypothesis. *American Journal of Psychology*, *115*(1), 21–32. https://doi.org/10.2307/1423672

Hoffman, H. G., Chambers, G. T., Meyer, W. J., Arceneaux, L. L., Russell, W. J., Seibel, E. J., … Patterson, D. R. (2011). Virtual reality as an adjunctive non-pharmacologic analgesic for acute burn pain during medical procedures. *Annals of Behavioral Medicine : A Publication of the Society of Behavioral Medicine*, *41*(2), 183–191. https://doi.org/10.1007/s12160-010-9248-7

Holland, J. C., Morrow, G. R., Schmale, A., Derogatis, L., Stefanek, M., Berenson, S., … Feldstein, M. (1991). A randomized clinical trial of alprazolam versus progressive muscle relaxation in cancer patients with anxiety and depressive symptoms. *Journal of Clinical Oncology*, *9*(6), 1004–1011. https://doi.org/10.1200/JCO.1991.9.6.1004

Holland, R. W., Hendriks, M., & Aarts, H. (2005). Smells like clean spirit. Nonconscious effects of scent on cognition and behavior. *Psychological Science*, *16*(9), 689–693. https://doi.org/10.1111/j.1467-9280.2005.01597.x

Hong, J. Y., Sunwoo, M. K., Ham, J. H., Lee, J. J., Lee, P. H., & Sohn, Y. H. (2015). Apathy and olfactory dysfunction in early Parkinson's disease. *Journal of Movement Disorders*, *8*(1), 21–25. https://doi.org/10.14802/jmd.14029

House, G., Burdea, G., Grampurohit, N., Polistico, K., Roll, D., Damiani, F., … Demesmin, D. (2016). A feasibility study to determine the benefits of upper extremity virtual rehabilitation therapy for coping with chronic pain post-cancer surgery. *British Journal of Pain*, *10*(4), 186–197. https://doi.org/10.1177/2049463716664370

Howard, D. R. (1976). Multivariate relationships between leisure activities and personality. *Research Quarterly of the American Alliance for Health, Physical Education and Recreation*, *47*(2), 226–237. https://doi.org/10.1080/10671315.1976.10615366

Hyland, M. E., Halpin, D. M. G., Blake, S., Seamark, C., Pinnuck, M., Ward, D., … Seamark, D. (2016). Preference for different relaxation techniques by COPD patients: Comparison between six techniques. *International Journal of COPD*, *11*(1), 2315–2319. https://doi.org/10.2147/COPD.S113108

Hu, X., & Wang, K. (2010, October). Personalized recommendation for virtual reality. In 2010 International Conference on Multimedia Technology (pp. 1-5). IEEE.

Indovina, P., Barone, D., Gallo, L., Chirico, A., De Pietro, G., & Antonio, G. (2018). Virtual Reality as a Distraction Intervention to Relieve Pain and Distress During Medical Procedures. *The Clinical Journal of Pain*, 1. https://doi.org/10.1097/AJP.0000000000000599

Jacobs, G. D., Rosenberg, P. A., Friedman, R., Matheson, J., Peavy, G. M., Domar, A. D., & Benson, H. (1993). Multifactor Behavioral Treatment of Chronic Sleep-Onset Insomnia Using Stimulus Control and the Relaxation Response: A Preliminary Study. *Behavior Modification*, *17*(4), 498–509. https://doi.org/10.1177/01454455930174005

Jacobs, T. L., Epel, E. S., Lin, J., Blackburn, E. H., Wolkowitz, O. M., Bridwell, D. A., … Saron, C. D. (2011). Intensive meditation training, immune cell telomerase activity, and psychological mediators. *Psychoneuroendocrinology*, *36*(5), 664–681. https://doi.org/10.1016/j.psyneuen.2010.09.010

Jacobson, E. (1938). *Progressive relaxation* (2nd ed). Retrieved from https://psycnet.apa.org/record/1938-04698-000

Jacobson, Edmund. (1987). Progressive Relaxation. *The American Journal of Psychology*, *100*(3/4), 522. https://doi.org/10.2307/1422693

Jahn, P., Lakowa, N., Landenberger, M., Vordermark, D., & Stoll, O. (2012). InterACTIV: An Exploratory Study of the Use of a Game Console to Promote Physical Activation of Hospitalized Adult Patients With Cancer. *Oncology Nursing Forum*, *39*(2), E84–E90. https://doi.org/10.1188/12.ONF.E84-E90

Jain, S., Shapiro, S. L., Swanick, S., Roesch, S. C., Mills, P. J., Bell, I., & Schwartz, G. E. R. (2007). A randomized controlled trial of mindfulness meditation versus relaxation training: Effects on distress, positive states of mind, rumination, and distraction. *Annals of Behavioral Medicine*, *33*(1), 11–21. https://doi.org/10.1207/s15324796abm3301_2

John, O. P., Naumann, L. P., & Soto, C. J. (2008). Paradigm shift to the integrative Big Five trait taxonomy: History, measurement, and conceptual issues. In O. P. John, R. W. Robins, & L. A. Pervin (Eds.), Handbook of personality: Theory and research (p. 114–158). The Guilford Press.

Johnson, B. N., & Sobel, N. (2007). Methods for building an olfactometer with known concentration outcomes. *Journal of Neuroscience Methods*, *160*(2), 231–245. https://doi.org/10.1016/j.jneumeth.2006.09.008

Jones, S., & Dawkins, S. (2018). The Sensorama Revisited: Evaluating the Application of Multi-sensory Input on the Sense of Presence in 360-Degree Immersive Film in Virtual Reality. In *Augmented Reality and Virtual Reality* (pp. 183–197).

Jung, Y.-H., Ha, T. M., Oh, C. Y., Lee, U. S., Jang, J. H., Kim, J., … Kang, D.-H. (2016). The Effects of an Online Mind-Body Training Program on Stress, Coping Strategies, Emotional Intelligence, Resilience and Psychological State. *PLOS ONE*, *11*(8), e0159841. https://doi.org/10.1371/journal.pone.0159841

Kabat-Zinn, J. (2003). Mindfulness-Based Interventions in Context: Past, Present, and Future. *Clinical Psychology: Science and Practice*, *10*(2), 144–156. https://doi.org/10.1093/clipsy.bpg016

Kaneda, M., Oyama, H., & Katsumata, N. (1999). VR Intervention Therapy for Emotion Related Cancer Chemotherapy Side Effects. *ICAT '99 The Virtual Reality Society of Japan.*, 16–18.

Kang, Y., Rahrig, H., Eichel, K., Niles, H. F., Rocha, T., Lepp, N. E., … Britton, W. B. (2018). Gender differences in response to a school-based mindfulness training intervention for early adolescents. *Journal of School Psychology*, *68*, 163–176. https://doi.org/10.1016/j.jsp.2018.03.004

Kapogiannis, A., Tsoli, S., & Chrousos, G. (2018a). Investigating the Effects of the Progressive Muscle Relaxation-Guided Imagery Combination on Patients with Cancer Receiving Chemotherapy Treatment: A Systematic Review of Randomized Controlled Trials. *Explore*, *14*(2), 137–143. https://doi.org/10.1016/j.explore.2017.10.008

Katterman, S. N., Kleinman, B. M., Hood, M. M., Nackers, L. M., & Corsica, J. A. (2014, April). Mindfulness meditation as an intervention for binge eating, emotional eating, and weight loss: A systematic review. *Eating Behaviors*, Vol. 15, pp. 197–204. https://doi.org/10.1016/j.eatbeh.2014.01.005

Kawai, T., & Noro, K. (1996). Psychological effect of stereoscopic 3-d images with fragrances. *Ergonomics*, *39*(11), 1364–1369.

https://doi.org/10.1080/00140139608964556

Kaye, J. (2004). Making scents: Aromatic output for HCI. *Interactions*, *1*(11), 48–61.

Keller, A. (2011, December 16). Attention and olfactory consciousness. *Frontiers in Psychology*, Vol. 2, p. 380. https://doi.org/10.3389/fpsyg.2011.00380

Keller, A. (2014). The evolutionary function of conscious information processing is revealed by its task-dependency in the olfactory system. *Frontiers in Psychology*, *5*(FEB), 62. https://doi.org/10.3389/fpsyg.2014.00062

Kemper, K. J., Lynn, J., & Mahan, J. D. (2015). What Is the Impact of Online Training in Mind–Body Skills? *Journal of Evidence-Based Complementary and Alternative Medicine*, *20*(4), 275–282. https://doi.org/10.1177/2156587215580882

Khan, R. M., Luk, C.-H., Flinker, A., Aggarwal, A., Lapid, H., Haddad, R., & Sobel, N. (2007). Predicting odor pleasantness from odorant structure: pleasantness as a reflection of the physical world. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *27*(37), 10015–10023. https://doi.org/10.1523/JNEUROSCI.1158-07.2007

Khor, W. S., Baker, B., Amin, K., Chan, A., Patel, K., & Wong, J. (2016). Augmented and virtual reality in surgery-the digital surgical environment: applications, limitations and legal pitfalls. *Annals of Translational Medicine*, *4*(23), 454. https://doi.org/10.21037/atm.2016.12.23

King, J. R. (1983). Have the scents to relax? *World Medicine*, *19*, 29–31.

Knasko, S. C. (1992). Ambient odor's effect on creativity, mood, and perceived health. *Chemical Senses*, *17*(1), 27–35. https://doi.org/10.1093/chemse/17.1.27

Kong, E., Monje, F. J., Hirsch, J., & Pollak, D. D. (2014, February). Learning not to fear: Neural correlates of learned safety. *Neuropsychopharmacology*, Vol. 39, pp. 515–527. https://doi.org/10.1038/npp.2013.191

Korpela, Kalevi M., Ylén, M., Tyrväinen, L., & Silvennoinen, H. (2008). Determinants of restorative experiences in everyday favorite places. *Health & Place*, *14*(4), 636–652.

https://doi.org/10.1016/j.healthplace.2007.10.008

Korpela, Kalevi Mikael, & Ylén, M. P. (2009). Effectiveness of Favorite-Place Prescriptions. *American Journal of Preventive Medicine*, *36*(5), 435–438. https://doi.org/10.1016/j.amepre.2009.01.022

Köster, E. P., & de Wijk, R. A. (1991). Olfactory Adaptation. In *The Human Sense of Smell* (pp. 199–215). https://doi.org/10.1007/978-3-642-76223-9_10

Kris, M. G., Gralla, R. J., Clark, R. A., Tyson, L. B., O'Connell, J. P., Wertheim, M. S., & Kelsen, D. P. (1985). Incidence, course, and severity of delayed nausea and vomiting following the administration of high-dose cisplatin. *Journal of Clinical Oncology*, *3*(10), 1379–1384. https://doi.org/10.1200/JCO.1985.3.10.1379

Krusemark, E. A., Novak, L. R., Gitelman, D. R., & Li, W. (2013). When the Sense of Smell Meets Emotion: Anxiety-State-Dependent Olfactory Processing and Neural Circuitry Adaptation. *Journal of Neuroscience*, *33*(39), 15324–15332. https://doi.org/10.1523/JNEUROSCI.1835-13.2013

Kyle, G., Graefe, A., Manning, R., & Bacon, J. (2004). Effects of place attachment on users' perceptions of social and environmental conditions in a natural setting. *Journal of Environmental Psychology*, *24*(2), 213–225. https://doi.org/10.1016/J.JENVP.2003.12.006

Lahart, I. M., Metsios, G. S., Nevill, A. M., & Carmichael, A. R. (2015). Physical activity, risk of death and recurrence in breast cancer survivors: A systematic review and meta-analysis of epidemiological studies. *Acta Oncologica*. https://doi.org/10.3109/0284186X.2014.998275

Laver, K. E., Lange, B., George, S., Deutsch, J. E., Saposnik, G., & Crotty, M. (2017). Virtual reality for stroke rehabilitation. *Cochrane Database of Systematic Reviews*, *11*, CD008349. https://doi.org/10.1002/14651858.CD008349.pub4

Lazar, S. W., George Bush, C., Gollub, R. L., Fricchione, G. L., Khalsa, G., Benson, H., … Hausdorf and, J. (2000). Functional brain mapping of the relaxation response and

meditation. *NEUROREPORT*, *11*.

Leigh-Hunt, N., Bagguley, D., Bash, K., Turner, V., Turnbull, S., Valtorta, N., & Caan, W. (2017, November 1). An overview of systematic reviews on the public health consequences of social isolation and loneliness. *Public Health*, Vol. 152, pp. 157–171. https://doi.org/10.1016/j.puhe.2017.07.035

León-Pizarro, C., Gich, I., Barthe, E., Rovirosa, A., Farrús, B., Casas, F., … Arcusa, A. (2007). A randomized trial of the effect of training in relaxation and guided imagery techniques in improving psychological and quality-of-life indices for gynecologic and breast brachytherapy patients. *Psycho-Oncology*, *16*(11), 971–979. https://doi.org/10.1002/pon.1171

Li, W. H., Chung, J. O., & Ho, E. K. (2011). The effectiveness of therapeutic play, using virtual reality computer games, in promoting the psychological well-being of children hospitalised with cancer. *Journal of Clinical Nursing*, *20*(15–16), 2135–2143. https://doi.org/10.1111/j.1365-2702.2011.03733.x

Lim, C. C., Devi, M. K., & Ang, E. (2011). Anxiety in women with breast cancer undergoing treatment: a systematic review. *International Journal of Evidence-Based Healthcare*, *9*, 215–235. https://doi.org/10.1111/j.1744-1609.2011.00221.x

Littel, M., Remijn, M., Tinga, A. M., Engelhard, I. M., & van den Hout, M. A. (2017). Stress Enhances the Memory-Degrading Effects of Eye Movements on Emotionally Neutral Memories. *Clinical Psychological Science*. https://doi.org/10.1177/2167702616687292

Lombard, M., & Ditton, T. (2006). At the Heart of It All: The Concept of Presence. *Journal of Computer-Mediated Communication*, *3*(2), 0–0. https://doi.org/10.1111/j.1083-6101.1997.tb00072.x

Lorig, T. S., Elmes, D. G., Zald, D. H., & Pardo, J. V. (1999). A computer-controlled olfactometer for fMRI and electrophysiological studies of olfaction. *Behavior Research Methods, Instruments, and Computers*, *31*(2), 370–375.

https://doi.org/10.3758/BF03207734

Luberto, C. M., Hall, D. L., Park, E. R., Haramati, A., & Cotton, S. (2020). A Perspective on the Similarities and Differences Between Mindfulness and Relaxation. *Global Advances in Health and Medicine*, *9*, 216495612090559. https://doi.org/10.1177/2164956120905597

Lundström, J. N., Gordon, A. R., Alden, E. C., Boesveldt, S., & Albrecht, J. (2010). Methods for building an inexpensive computer-controlled olfactometer for temporally-precise experiments. *International Journal of Psychophysiology*, *78*(2), 179–189. https://doi.org/10.1016/j.ijpsycho.2010.07.007

Ma, X., Yue, Z. Q., Gong, Z. Q., Zhang, H., Duan, N. Y., Shi, Y. T., … Li, Y. F. (2017). The effect of diaphragmatic breathing on attention, negative affect and stress in healthy adults. *Frontiers in Psychology*, *8*(JUN). https://doi.org/10.3389/fpsyg.2017.00874

Macinko, J., & Upchurch, D. M. (2019). Factors Associated with the Use of Meditation, U.S. Adults 2017. *Journal of Alternative and Complementary Medicine*, *25*(9), 920–927. https://doi.org/10.1089/acm.2019.0206

Maggioni, E, Cobden, R., & Obrist, M. (2019). OWidgets: A Toolkit To Enable Smell-based Experience Design. *International Journal of Human - Computer Studies*, *In Press*.

Maggioni, Emanuela, Cobden, R., Dmitrenko, D., & Obrist, M. (2018). *Smell-O-Message: Integration of Olfactory Notifications into a Mes-saging Application to Improve Users' Performance*. https://doi.org/10.1145/3242969.3242975

Malloy, K. M., & Milling, L. S. (2010). The effectiveness of virtual reality distraction for pain reduction: a systematic review. *Clinical Psychology Review*, *30*(8), 1011–1018. https://doi.org/10.1016/j.cpr.2010.07.001

Manzoni, G. M., Pagnini, F., Castelnuovo, G., & Molinari, E. (2008). Relaxation training for anxiety: A ten-years systematic review with meta-analysis. *BMC Psychiatry*, *8*. https://doi.org/10.1186/1471-244X-8-41

Maples-Keller, J. L., Yasinski, C., Manjin, N., & Rothbaum, B. O. (2017). Virtual Reality-

Enhanced Extinction of Phobias and Post-Traumatic Stress. *Neurotherapeutics : The Journal of the American Society for Experimental NeuroTherapeutics*, *14*(3), 554–563. https://doi.org/10.1007/s13311-017-0534-y

Marissen, M. A. E., Franken, I. H. A., Blanken, P., van den Brink, W., & Hendriks, V. M. (2007). Cue Exposure Therapy for the Treatment of Opiate Addiction: Results of a Randomized Controlled Clinical Trial. *Psychotherapy and Psychosomatics*, *76*(2), 97–105. https://doi.org/10.1159/000097968

Mark, B.-L., Habel, U., Brehl, A.-K., Freiherr, J., Losleben, K., Schneider, F., … Kohn, N. (2018). Implicit affective rivalry: A behavioral and fMRI study combining olfactory and auditory stimulation. *Frontiers in Behavioral Neuroscience*, *12*(December), 313. https://doi.org/10.3389/FNBEH.2018.00313

Marquess, M., Johnston, S. P., Williams, N. L., Giordano, C., Leiby, B. E., Hurwitz, M. D., … Den, R. B. (2017). A pilot study to determine if the use of a virtual reality education module reduces anxiety and increases comprehension in patients receiving radiation therapy. *Journal of Radiation Oncology*, *6*(3), 317–322. https://doi.org/10.1007/s13566-017-0298-3

Martin, G. N. (1996). Olfactory remediation: Current evidence and possible applications. *Social Science and Medicine*, *43*(1), 63–70. https://doi.org/10.1016/0277-9536(95)00334-7

Matsukura, H., Yoneda, T., & Ishida, H. (2013). Smelling Screen: Development and Evaluation of an Olfactory Display System for Presenting a Virtual Odor Source. *IEEE Transactions on Visualization and Computer Graphics*, *19*(4), 606–615. https://doi.org/10.1109/TVCG.2013.40

Matsumoto, M., & Smith, J. C. (2001). Progressive Muscle Relaxation, Breathing Exercises, and ABC Relaxation Theory. In *J Clin Psychol* (Vol. 57). Retrieved from https://onlinelibrary.wiley.com/doi/pdf/10.1002/jclp.1117

Mikolasek, M., Berg, J., Witt, C. M., & Barth, J. (2018). Effectiveness of Mindfulness- and

Relaxation-Based eHealth Interventions for Patients with Medical Conditions: a Systematic Review and Synthesis. *International Journal of Behavioral Medicine*, *25*(1). https://doi.org/10.1007/s12529-017-9679-7

Mirams, L., Poliakoff, E., Brown, R. J., & Lloyd, D. M. (2013). Brief body-scan meditation practice improves somatosensory perceptual decision making. *Consciousness and Cognition*. https://doi.org/10.1016/j.concog.2012.07.009

Mitchell, A. J., Chan, M., Bhatti, H., Halton, M., Grassi, L., Johansen, C., & Meader, N. (2011). Prevalence of depression, anxiety, and adjustment disorder in oncological, haematological, and palliative-care settings: a meta-analysis of 94 interview-based studies. *The Lancet Oncology*, *12*(2), 160–174. https://doi.org/10.1016/S1470-2045(11)70002-X

Monzani, D., Steca, P., Greco, A., D'Addario, M., Cappelletti, E., & Pancani, L. (2015). The situational version of the brief COPE: Dimensionality and relationships with goal-related variables. *Europe's Journal of Psychology*, *11*(2), 295–310. https://doi.org/10.5964/ejop.v11i2.935

Morin, C. M., Gaulier, B., Barry, T., & Kowatch, R. A. (1992). Patients' acceptance of psychological and pharmacological therapies for insomnia. *Sleep*, *15*(4), 302–305. https://doi.org/10.1093/sleep/15.4.302

Morina, N., Ijntema, H., Meyerbröker, K., Emmelkamp, P. M. G., Fodor, L. A., Coteţ, C. D., … Muhlberger, A. (2017). Virtual reality exposure therapy in flight anxiety: A quantitative meta-analysis. *Frontiers in Psychology*, *18*(1), 113–123. https://doi.org/10.1097/HRP.0000000000000138

Morris, A. (2017). Obesity: Olfactory senses linked to metabolism. *Nature Reviews Endocrinology 2017 13:9*.

Morrison, F. G., Dias, B. G., & Ressler, K. J. (2015). Extinction reverses olfactory fear-conditioned increases in neuron number and glomerular size. *Proceedings of the National Academy of Sciences*, *112*(41), 12846–12851.

https://doi.org/10.1073/pnas.1505068112

Moss, M., Cook, J., Wesnes, K., & Duckett, P. (2003). Aromas of rosemary and lavender essential oils differentially affect cognition and mood in healthy adults. *International Journal of Neuroscience*, *113*(1), 15–38. https://doi.org/10.1080/00207450390161903

Munyan III, B. G., Neer, S. M., Beidel, D. C., & Jentsch, F. (2016). Olfactory stimuli increase presence in virtual environments. *PLoS ONE*, *11*(6), 1–19. https://doi.org/10.1021/je00028a022

Murata, T., Takahashi, T., Hamada, T., Omori, M., Kosaka, H., Yoshida, H., & Wada, Y. (2004). Individual Trait Anxiety Levels Characterizing the Properties of Zen Meditation. *Neuropsychobiology*, *50*(2), 189–194. https://doi.org/10.1159/000079113

Nakao, M., Fricchione, G., Myers, P., Zuttermeister, P. C., Baim, M., Mandle, C. L., … Benson, H. (2001). Anxiety is a good indicator for somatic symptom reduction through behavioral medicine intervention in a mind/body medicine clinic. *Psychotherapy and Psychosomatics*, *70*(1), 50–57. https://doi.org/10.1159/000056225

Nordahl, H., Hjemdal, O., Hagen, R., Nordahl, H. M., & Wells, A. (2019). What lies beneath trait-anxiety? Testing the self-regulatory executive function model of vulnerability. *Frontiers in Psychology*, *10*(JAN), 122. https://doi.org/10.3389/fpsyg.2019.00122

Obrist, M., Gatti, E., Maggioni, E., Vi, C. T., & Velasco, C. (2017). Multisensory Experiences in HCI. *IEEE Multimedia*, *24*(2), 9–13. https://doi.org/10.1109/MMUL.2017.33

Obrist, M., Tuch, A. N., & Hornbaek, K. (2014). Opportunities for odor: Experiences with Smell and Implications for Technology. *Proceedings of the 32nd Annual ACM Conference on Human Factors in Computing Systems - CHI '14*, 2843–2852. https://doi.org/10.1145/2556288.2557008

Oeffinger, K. C., Fontham, E. T. H., Etzioni, R., Herzig, A., Michaelson, J. S., Shih, Y. C. T., … Wender, R. (2015). Breast cancer screening for women at average risk: 2015 Guideline update from the American cancer society. *JAMA - Journal of the American*

*Medical Association*. https://doi.org/10.1001/jama.2015.12783

Olatunji, B. O., Deacon, B. J., Abramowitz, J. S., & Valentiner, D. P. (2007). Body Vigilance in Nonclinical and Anxiety Disorder Samples: Structure, Correlates, and Prediction of Health Concerns. *Behavior Therapy*, *38*(4), 392–401. https://doi.org/10.1016/j.beth.2006.09.002

Öst, L. G. (1987). Applied relaxation: Description of a coping technique and review of controlled studies. *Behaviour Research and Therapy*, *25*(5), 397–409. https://doi.org/10.1016/0005-7967(87)90017-9

Oyama, H, Ohsuga, M., Tatsuno, Y., & Katsumata, N. (1999). Evaluation of the psycho-oncological effectiveness of the bedside wellness system. *Cyberpsychology & Behavior : The Impact of the Internet, Multimedia and Virtual Reality on Behavior and Society*, *2*(1), 81–84. https://doi.org/10.1089/cpb.1999.2.81

Oyama, Hiroshi. (1997). Virtual reality for the palliative care of cancer. In G. Riva (Ed.), *Virtual reality in neuro-psycho-physiology* (pp. 87–94). Amsterdam: IOS Press.

Oyama, Hiroshi, Kaneda, M., Katsumata, N., Akechi, T., & Ohsuga, M. (2000). Using the bedside wellness system during chemotherapy decreases fatigue and emesis in cancer patients. *Journal of Medical Systems*, *24*(3), 173–182. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10984871

Pachman, D. R., Barton, D. L., Swetz, K. M., & Loprinzi, C. L. (2012). Troublesome symptoms in cancer survivors: fatigue, insomnia, neuropathy, and pain. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology*, *30*(30), 3687–3696. https://doi.org/10.1200/JCO.2012.41.7238

Parsons, T. D., & Reinebold, J. L. (2012). *Adaptive Virtual Environments for Neuropsychological Assessment in Serious Games*. Retrieved from http://psychology.unt.edu/~tparsons/PDF/Parsons_AVEs for neuropsychological assessment.pdf

Parsons, T. D., Rizzo, A. A., Rogers, S., & York, P. (2009). Virtual reality in paediatric

rehabilitation: a review. *Developmental Neurorehabilitation*, *12*(4), 224–238. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/19842822

Pause, B. M., Sojka, B., Krauel, K., Fehm-Wolfsdorf, G., & Ferstl, R. (1996). Olfactory information processing during the course of the menstrual cycle. *Biological Psychology*, *44*(1), 31–54. https://doi.org/10.1016/S0301-0511(96)05207-6

Pedrabissi, L., & Santinello, M. (1989). Verifica della validità dello STAI forma Y di Spielberger. . *Giunti Organizzazioni Speciali*, *191–192*, 11–14. Retrieved from https://psycnet.apa.org/record/1991-73411-001

Peng, C.-K., Henry, I. C., Mietus, J. E., Hausdorff, J. M., Khalsa, G., Benson, H., … Rey, H. A. (2004). Heart rate dynamics during three forms of meditation. *International Journal of Cardiology*, *95*, 19–27. https://doi.org/10.1016/j.ijcard.2003.02.006

Penn, P. R., Rose, F. D., & Johnson, D. A. (2009). Virtual enriched environments in paediatric neuropsychological rehabilitation following traumatic brain injury: Feasibility, benefits and challenges. *Developmental Neurorehabilitation*, *12*(1), 32–43. https://doi.org/10.1080/17518420902739365

Petrocchi, N., Tenore, K., Couyoumdjian, A., & Gragnani, A. (2014). he Anxiety Sensitivity Index-3: Factor structure and psychometric properties in Italian clinical and non-clinical samples. *Applied Psychology Bulletin*, *269*(62), 53–64.

Pizzoli, S. F. M., Mazzocco, K., Triberti, S., Monzani, D., Alcañiz Raya, M. L., & Pravettoni, G. (2019). User-Centered Virtual Reality for Promoting Relaxation: An Innovative Approach. *Frontiers in Psychology*, *10*, 479. https://doi.org/10.3389/fpsyg.2019.00479

Pizzoli, S. F., Triberti, S., Monzani, D., Mazzocco, K., Kufel, E., Porebiak, M., & Pravettoni, G. (2019). Comparison of relaxation techniques in virtual reality for breast cancer patients. *Proceedings of the 2019 5th Experiment at International Conference, Exp.at 2019*, 348–351. https://doi.org/10.1109/EXPAT.2019.8876542

Pizzoli, S. M. F., Marzorati, C., Mazzoni, D., & Pravettoni, G. (2020). An Internet-Based Intervention to Alleviate Stress During Social Isolation With Guided Relaxation and

Meditation: Protocol for a Randomized Controlled Trial. *JMIR Research Protocols*, *9*(6), e19236. https://doi.org/10.2196/19236

Poellinger, A., Thomas, R., Lio, P., Lee, A., Makris, N., Rosen, B. R., & Kwong, K. K. (2001). Activation and Habituation in Olfaction—An fMRI Study. *NeuroImage*, *13*(4), 547–560. https://doi.org/10.1006/NIMG.2000.0713

Pollatos, O., Kopietz, R., Linn, J., Albrecht, J., Sakar, V., Anzinger, A., … Wiesmann, M. (2007). Emotional Stimulation Alters Olfactory Sensitivity and Odor Judgment. *Chemical Senses*, *32*(6), 583–589. https://doi.org/10.1093/chemse/bjm027

Porges, S. W. (2001). The polyvagal theory: Phylogenetic substrates of a social nervous system. *International Journal of Psychophysiology*, *42*(2), 123–146. https://doi.org/10.1016/S0167-8760(01)00162-3

Potvin, O., Bergua, V., Meillon, C., Le Goff, M., Bouisson, J., Dartigues, J. F., & Amieva, H. (2011). Norms and associated factors of the STAI-Y State anxiety inventory in older adults: Results from the PAQUID study. *International Psychogeriatrics*, *23*(6), 869–879. https://doi.org/10.1017/S1041610210002358

Pourmand, A., Davis, S., Lee, D., Barber, S., & Sikka, N. (2017). Emerging Utility of Virtual Reality as a Multidisciplinary Tool in Clinical Medicine. *Games for Health Journal*, *6*(5), 263–270. https://doi.org/10.1089/g4h.2017.0046

Pozza, A., & Dèttore, D. (2015). Psychometric Evidence of the Italian Anxiety Sensitivity Index-3 (ASI-3) in Patients with Anxiety Disorders and Psychosis. *Research in Psychology and Behavioral Sciences*, *3*(1), 7–17. https://doi.org/10.12691/rpbs-3-1-3

Rainforth, M. V., Schneider, R. H., Nidich, S. I., Gaylord-King, C., Salerno, J. W., & Anderson, J. W. (2007, December). Stress reduction programs in patients with elevated blood pressure: A systematic review and meta-analysis. *Current Hypertension Reports*, Vol. 9, pp. 520–528. https://doi.org/10.1007/s11906-007-0094-3

Renzi, C., Riva, S., Masiero, M., & Pravettoni, G. (2016). The choice dilemma in chronic hematological conditions: Why choosing is not only a medical issue? A psycho-

cognitive perspective. *Critical Reviews in Oncology/Hematology*, *99*, 134–140. https://doi.org/10.1016/j.critrevonc.2015.12.010

Renzi, D. A. (1985). State-Trait Anxiety Inventory. *Measurement and Evaluation in Counseling and Development*. https://doi.org/10.1080/07481756.1985.12022795

Rey, B., Montesa, J., Alcañiz, M., Baños, R., & Botella, C. (2005). A Preliminary Study on the Use of an Adaptive Display for the Treatment of Emotional Disorders. *PsychNology Journal*, *3*(1), 101–112. Retrieved from http://www.psychnology.org/File/PNJ3(1)/PSYCHNOLOGY_JOURNAL_3_1_REY.pdf

Richards, D., & Richardson, T. (2012, June). Computer-based psychological treatments for depression: A systematic review and meta-analysis. *Clinical Psychology Review*, Vol. 32, pp. 329–342. https://doi.org/10.1016/j.cpr.2012.02.004

Riera, C. E., Tsaousidou, E., Halloran, J., Follett, P., Hahn, O., Pereira, M. M. A., … Dillin, A. (2017). The Sense of Smell Impacts Metabolic Health and Obesity. *Cell Metabolism*, *26*(1), 198-211.e5. https://doi.org/10.1016/j.cmet.2017.06.015

Rinaldi, L., Maggioni, E., Olivero, N., Maravita, A., & Girelli, L. (2018). Smelling the space around us: Odor pleasantness shifts visuospatial attention in humans. *Emotion*, *18*(7), 971–979. https://doi.org/10.1037/emo0000335

Risso, P., Covarrubias Rodriguez, M., Bordegoni, M., & Gallace, A. (2018). Development and Testing of a Small-Size Olfactometer for the Perception of Food and Beverages in Humans. *Frontiers in Digital Humanities*, *5*, 7. https://doi.org/10.3389/fdigh.2018.00007

Riva, G., Davide, F., & IJsselsteijn, W. A. (2003). *Being there : concepts, effects and measurements of user presence in synthetic environments*. Retrieved from http://repository.tue.nl/513562fc-4a12-44e1-a82a-8cb30f06e40c

Rizzo, A. “Skip,” Difede, J., Rothbaum, B. O., Reger, G., Spitalnick, J., Cukor, J., & Mclay, R. (2010). Development and early evaluation of the Virtual Iraq/Afghanistan exposure

therapy system for combat-related PTSD. *Annals of the New York Academy of Sciences*, *1208*(1), 114–125. https://doi.org/10.1111/j.1749-6632.2010.05755.x

Rizzo, A. 'Skip,' & Shilling, R. (2018). Clinical Virtual Reality tools to advance the prevention, assessment, and treatment of PTSD. *European Journal of Psychotraumatology*, *8*(sup5), 1414560. https://doi.org/10.1080/20008198.2017.1414560

Rose, T., Nam, C. S., & Chen, K. B. (2018). Immersion of virtual reality for rehabilitation - Review. *Applied Ergonomics*, *69*, 153–161. https://doi.org/10.1016/J.APERGO.2018.01.009

Rosenblatt, L. (2006). Being the monster: women's narratives of body and self after treatment for breast cancer. *Medical Humanities*, *32*(1), 53–56.

Sarafoleanu, C., Mella, C., Georgescu, M., & Perederco, C. (2009). The importance of the olfactory sense in the human behavior and evolution. *Journal of Medicine and Life*, *2*(2), 196–198. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/20108540

Sauer-Zavala, S. E., Walsh, E. C., Eisenlohr-Moul, T. A., & Lykins, E. L. B. (2013). Comparing Mindfulness-Based Intervention Strategies: Differential Effects of Sitting Meditation, Body Scan, and Mindful Yoga. *Mindfulness*. https://doi.org/10.1007/s12671-012-0139-9

Savic, I., Berglund, H., Gulyas, B., & Roland, P. (2001). Smelling of odorous sex hormone-like compounds causes sex-differentiated hypothalamic activations in humans. *Neuron*, *31*(4), 661–668. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11545724

Scheffler, M., Koranyi, S., Meissner, W., Strauß, B., & Rosendahl, J. (2017). Efficacy of non-pharmacological interventions for procedural pain relief in adults undergoing burn wound care: A systematic review and meta-analysis of randomized controlled trials. *Burns : Journal of the International Society for Burn Injuries*. https://doi.org/10.1016/j.burns.2017.11.019

Scheufele, P. M. (2000). Effects of progressive relaxation and classical music on

measurements of attention, relaxation, and stress responses. *Journal of Behavioral Medicine*. https://doi.org/10.1023/A:1005542121935

Schmidt, N. B., Lerew, D. R., & Trakowski, J. H. (1997). Body vigilance in panic disorder: Evaluating attention to bodily perturbations. *Journal of Consulting and Clinical Psychology*, *65*(2), 214–220. https://doi.org/10.1037/0022-006X.65.2.214

Schneider, S. M., & Hood, L. E. (2007). Virtual Reality: A Distraction Intervention for Chemotherapy. *Oncology Nursing Forum*, *34*(1), 39–46. https://doi.org/10.1188/07.ONF.39-46

Schneider, S. M., Prince-Paul, M., JoAllen, M., Silverman, P., & Talaba, D. (2004). Virtual Reality as a Distraction Intervention for Women Receiving Chemotherapy. *Oncology Nursing Forum*, *31*(1), 81–88. https://doi.org/10.1188/04.ONF.81-88

Seigneuric, A., Durand, K., Jiang, T., Baudouin, J.-Y., & Schaal, B. (2010). The Nose Tells it to the Eyes: Crossmodal Associations between Olfaction and Vision. *Perception*, *39*(11), 1541–1554. https://doi.org/10.1068/p6740

Serrano, B., Baños, R. M., & Botella, C. (2016). Virtual reality and stimulation of touch and smell for inducing relaxation: A randomized controlled trial. *Computers in Human Behavior*, *55*, 1–8. https://doi.org/10.1016/J.CHB.2015.08.007

Shanahan, L. K., Gjorgieva, E., Paller, K. A., Kahnt, T., & Gottfried, J. A. (2018). Odor-evoked category reactivation in human ventromedial prefrontal cortex during sleep promotes memory consolidation. *ELife*, *7*. https://doi.org/10.7554/eLife.39681

Shapiro, F. (2001). *Eye movement desensitization and reprocessing (EMDR) therapy : basic principles, protocols, and procedures* (2nd ed.). Retrieved from https://books.google.it/books?hl=it&lr=&id=7pk8DwAAQBAJ&oi=fnd&pg=PP1&dq=shapiro+calm+safe+place&ots=YsCHsnTcXt&sig=X7MBqr1_GBL-4WrcxBmgM7AIu-E#v=onepage&q=shapiro calm safe place&f=false

Shin, H., & Kim, K. (2015). Virtual reality for cognitive rehabilitation after brain injury: a systematic review. *Journal of Physical Therapy Science*, *27*(9), 2999–3002.

https://doi.org/10.1589/jpts.27.2999

Slater, M., Spanlang, B., Sanchez-Vives, M. V., & Blanke, O. (2010). First person experience of body transfer in virtual reality. *PLoS ONE*, *5*. https://doi.org/10.1371/journal.pone.0010564

Slater, M., & Wilbur, S. (1997). A Framework for Immersive Virtual Environments (FIVE): Speculations on the Role of Presence in Virtual Environments. *Presence: Teleoperators and Virtual Environments*, *6*(6), 603–616. https://doi.org/10.1162/pres.1997.6.6.603

Slovic, P., Peters, E., Finucane, M. L., & MacGregor, D. G. (2005, July). Affect, risk, and decision making. *Health Psychology*, Vol. 24. https://doi.org/10.1037/0278-6133.24.4.S35

Smeets, M. A. M., Veldhuizen, M. G., Galle, S., Gouweloos, J., de Haan, A.-M. J. A., Vernooij, J., … Kroeze, J. H. A. (2009). Sense of smell disorder and health-related quality of life. *Rehabilitation Psychology*, *54*(4), 404–412. https://doi.org/10.1037/a0017502

Smith, J. C. (1999). *ABC relaxation training: An evidence-based approach.* New York, NY: Springer New York.

Sobel, N., Prabhakaran, V., Desmond, J. E., Glover, G. H., Sullivan, E. V, & Gabrieli, J. D. E. (1997). A method for functional magnetic resonance imaging of olfaction. In *Journal of Neuroscience Methods* (Vol. 78). Retrieved from https://ac.els-cdn.com/S0165027097001404/1-s2.0-S0165027097001404-main.pdf?_tid=9157851c-7e1e-4a0d-9906-7800606063ce&acdnat=1548772310_ecdf67dbe13a1cc8c535d40a22596097

Solberg Nes, L., & Segerstrom, S. C. (2006). Dispositional optimism and coping: A meta-analytic review. *Personality and Social Psychology Review*, *10*(3), 235–251. https://doi.org/10.1207/s15327957pspr1003_3

Song, C., Ikei, H., Lee, J., Park, B. J., Kagawa, T., & Miyazaki, Y. (2013). Individual differences in the physiological effects of forest therapy based on Type A and Type B

behavior patterns. *Journal of Physiological Anthropology*, *32*(1), 1–7. https://doi.org/10.1186/1880-6805-32-14

Sowndhararajan, K., & Kim, S. (2016). Influence of fragrances on human psychophysiological activity: With special reference to human electroencephalographic response. *Scientia Pharmaceutica*, *84*(4), 724–751. https://doi.org/10.3390/scipharm84040724

Spanakis, E. G., Santana, S., Tsiknakis, M., Marias, K., Sakkalis, V., Teixeira, A., … Tziraki, C. (2016). Technology-Based Innovations to Foster Personalized Healthy Lifestyles and Well-Being: A Targeted Review. *Journal of Medical Internet Research*, *18*(6), e128. https://doi.org/10.2196/jmir.4863

Spencer, B. S. (2005). Incorporating the sense of smell into haptic surgical simulators. *Studies in Health Technology and Informatics*, *114*, 54–62. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15923761

Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). *State-Trait Anxiety Inventory for Adults Sampler Set Manual, Instrument and Scoring Guide*. Retrieved from www.mindgarden.com.

Suls, J., & Fletcher, B. (1985). The relative efficacy of avoidant and nonavoidant coping strategies: A meta-analysis. *Health Psychology*, *4*(3), 249–288. https://doi.org/10.1037//0278-6133.4.3.249

Taylor, S., Zvolensky, M. J., Cox, B. J., Deacon, B., Heimberg, R. G., Ledley, D. R., … Cardenas, S. J. (2007). Robust Dimensions of Anxiety Sensitivity: Development and Initial Validation of the Anxiety Sensitivity Index-3. *Psychological Assessment*, *19*, 176–188. https://doi.org/10.1037/1040-3590.19.2.176

Teo, W.-P., Muthalib, M., Yamin, S., Hendy, A. M., Bramstedt, K., Kotsopoulos, E., … Ayaz, H. (2016). Does a Combination of Virtual Reality, Neuromodulation and Neuroimaging Provide a Comprehensive Platform for Neurorehabilitation? – A Narrative Review of the Literature. *Frontiers in Human Neuroscience*, *10*, 284.

https://doi.org/10.3389/fnhum.2016.00284

Theobald, D. E. (2004). Cancer pain, fatigue, distress, and insomnia in cancer patients. *Clinical Cornerstone*, *6 Suppl 1D*, S15-21. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/15675653

Thoma, M. V., Mewes, R., & Nater, U. M. (2018). Preliminary evidence: The stress-reducing effect of listening to water sounds depends on somatic complaints. *Medicine (United States)*, *97*(8). https://doi.org/10.1097/MD.0000000000009851

Tinsley, H. E. A., & Eldredge, B. D. (1995). Psychological Benefits of Leisure Participation: A Taxonomy of Leisure Activities Based on Their Need-Gratifying Properties. *Journal of Counseling Psychology*, *42*(2), 123–132. https://doi.org/10.1037/0022-0167.42.2.123

Tinsley, H. E. A., & Johnson, T. L. (1984). A Preliminary Taxonomy of Leisure Activities. *Journal of Leisure Research*, *16*(3), 234–244. https://doi.org/10.1080/00222216.1984.11969588

Tobin, D. L., Holroyd, K. A., Reynolds, R. V., & Wigal, J. K. (1989). The hierarchical factor structure of the coping strategies inventory. *Cognitive Therapy and Research*, *13*(4), 343–361. https://doi.org/10.1007/BF01173478

Toivonen, K. I., Zernicke, K., & Carlson, L. E. (2017, August 1). Web-based mindfulness interventions for people with physical health conditions: Systematic review. *Journal of Medical Internet Research*, Vol. 19. https://doi.org/10.2196/jmir.7487

Triberti, S., Chirico, A., La Rocca, G., & Riva, G. (2017). Developing emotional design: Emotions as cognitive processes and their role in the design of interactive technologies. Frontiers in Psychology, 8, 1773.

Triberti S., Brivio E. (2020) User-Centered Design Approaches and Methods for P5 eHealth. In: Pravettoni G., Triberti S. (eds) P5 eHealth: An Agenda for the Health Technologies of the Future. Springer, Cham. https://doi.org/10.1007/978-3-030-27994-3_9

Tsuda, K., Sudo, K., Goto, G., Takai, M., Itokawa, T., Isshiki, T., … Komatsu, T. (2016). A

Feasibility Study of Virtual Reality Exercise in Elderly Patients with Hematologic Malignancies Receiving Chemotherapy. *Internal Medicine*, *55*(4), 347–352. https://doi.org/10.2169/internalmedicine.55.5275

Upchurch, D. M., & Johnson, P. J. (2019). Gender differences in prevalence, patterns, purposes, and perceived benefits of meditation practices in the United States. *Journal of Women's Health*, *28*(2), 135–142. https://doi.org/10.1089/jwh.2018.7178

Van Hartevelt, T. J., & Kringelbach, M. L. (2012). Chapter 34 – The Olfactory System. *The Human Nervous System*, 1219–1238. https://doi.org/10.1016/B978-0-12-374236-0.10034-3

Vasterling, J., Jenkins, R. A., Tope, D. M., & Burish, T. G. (1993). Cognitive distraction and relaxation training for the control of side effects due to cancer chemotherapy. *J Behav Med*, *16*(1), 65–80.

Vergani, L., Marton, G., Pizzoli, S. F. M., Monzani, D., Mazzocco, K., & Pravettoni, G. (2019). Training Cognitive Functions Using Mobile Apps in Breast Cancer Patients: Systematic Review. *JMIR MHealth and UHealth*, *7*(3), e10855. https://doi.org/10.2196/10855

Villani, D. (2006). Coping with stress using virtual reality. *Annual Review of CyberTherapy and Telemedicine*, *4*.

Villani, D., Riva, F., & Riva, G. (2007a). New technologies for relaxation: The role of presence. *International Journal of Stress Management*, *14*(3), 260–274. https://doi.org/10.1037/1072-5245.14.3.260

Villani, D., Riva, F., & Riva, G. (2007b). New Technologies for Relaxation: The Role of Presence. *Psychological Association*, *14*(3), 260–274. https://doi.org/10.1037/1072-5245.14.3.260

Vinci, C., Reblin, M., Jim, H., Pidala, J., Bulls, H., & Cutolo, E. (2018). Understanding preferences for a mindfulness-based stress management program among caregivers of hematopoietic cell transplant patients. *Complementary Therapies in Clinical Practice*,

*33*, 164–169. https://doi.org/10.1016/j.ctcp.2018.10.007

Walla, P. (2008, February). Olfaction and its dynamic influence on word and face processing: Cross-modal integration. *Progress in Neurobiology*, Vol. 84, pp. 192–209. https://doi.org/10.1016/j.pneurobio.2007.10.005

Waltemate, T., Gall, D., Roth, D., Botsch, M., & Latoschik, M. E. (2018). The impact of avatar personalization and immersion on virtual body ownership, presence, and emotional response. IEEE transactions on visualization and computer graphics, 24(4), 1643-1652.

Wang, M., & Reid, D. (2011). Virtual reality in pediatric neurorehabilitation: attention deficit hyperactivity disorder, autism and cerebral palsy. *Neuroepidemiology*, *36*(1), 2–18. https://doi.org/10.1159/000320847

Wang, X., Smith, C., Ashley, L., & Hyland, M. E. (2019). Tailoring Self-Help Mindfulness and Relaxation Techniques for Stroke Survivors: Examining Preferences, Feasibility and Acceptability. *Frontiers in Psychology*, *10*(FEB), 391. https://doi.org/10.3389/fpsyg.2019.00391

Warrenburg, S. (2005). Effects of Fragrance on Emotions: Moods and Physiology. *Chemical Senses*, *30*(Supplement 1), i248–i249. https://doi.org/10.1093/chemse/bjh208

Wei, N., Huang, B. chao, Lu, S. jia, Hu, J. bo, Zhou, X. yi, Hu, C. chan, … Hu, S. hua. (2020, May 1). Efficacy of internet-based integrated intervention on depression and anxiety symptoms in patients with COVID-19. *Journal of Zhejiang University: Science B*, Vol. 21, pp. 400–404. https://doi.org/10.1631/jzus.B2010013

Wiederhold, B. K., Riva, G., & Gutiérrez-Maldonado, J. (2016). Virtual Reality in the Assessment and Treatment of Weight-Related Disorders. *Cyberpsychology, Behavior and Social Networking*, *19*(2), 67–73. https://doi.org/10.1089/cyber.2016.0012

Wielgosz, J., Goldberg, S. B., Kral, T. R. A., Dunne, J. D., & Davidson, R. J. (2019). Mindfulness Meditation and Psychopathology. *Annual Review of Clinical Psychology*, *15*(1), 285–316. https://doi.org/10.1146/annurev-clinpsy-021815-093423

Willander, J., & Larsson, M. (2006). Smell your way back to childhood: Autobiographical odor memory. *Psychonomic Bulletin & Review*, *13*(2), 240–244.

Willander, J., & Larsson, M. (2007). Olfaction and emotion: the case of autobiographical memory. *Memory & Cognition*, *35*(7), 1659–1663. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/18062543

Williams, A. L., Van Ness, P., Dixon, J., & McCorkle, R. (2012). Barriers to meditation by gender and age among cancer family caregivers. *Nursing Research*, *61*(1), 22–27. https://doi.org/10.1097/NNR.0b013e3182337f4d

Wolitzky, K., Fivush, R., Zimand, E., Hodges, L., & Rothbaum, B. O. (2005). Effectiveness of virtual reality distraction during a painful medical procedure in pediatric oncology patients. *Psychology & Health*, *20*(6), 817–824. https://doi.org/10.1080/14768320500143339

World Health Organization. (2020). Coronavirus. Retrieved from WHO website: https://www.who.int/health-topics/coronavirus#tab=tab_1

Yeshurun, Y., & Sobel, N. (2010). An Odor is Not Worth a Thousand Words: From Multidimensional Odors to Unidimensional Odor Objects. *Annual Review of Psychology*, *61*(1), 219–241. https://doi.org/10.1146/annurev.psych.60.110707.163639

Zebrack, B., Kayser, K., Sundstrom, L., Savas, S. A., Henrickson, C., Acquati, C., & Tamas, R. L. (2015). Psychosocial distress screening implementation in cancer care:An analysis of adherence, responsiveness, and acceptability. *Journal of Clinical Oncology*, *33*(10), 1165–1170. https://doi.org/10.1200/JCO.2014.57.4020

Zhang, Y., Luo, Y., & Zeng, Y. (2017, July 10). Meta-analysis of meditative/relaxation-based interventions for cognitive impairment in cancer patient. *International Journal of Nursing Sciences*, Vol. 4, pp. 322–327. https://doi.org/10.1016/j.ijnss.2017.03.010

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