Translating the Effects of Environmental Enrichment on Stress and Wound Healing to Human Populations

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A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy in Health Psychology, the University of Auckland, 2020.

Abstract

Environmental enrichment has been studied extensively in animals; however, little research has been conducted in humans. This thesis aimed to investigate whether the effects of environmental enrichment on stress and wound healing seen in animal research could translate to humans. Four studies and one scoping review were conducted. Theme one of the thesis studied sensory enrichment (music, soft blankets) and social enrichment (the companion robot Paro), whereas theme two studied visual artworks.

In the first theme, two experimental studies examined the effects of music and Paro on skin barrier recovery from a tape-stripping wound. The first study found no significant effects on healing in a healthy, non-stressed sample compared to an active control. The second study found that after exposure to a stressor, interacting with Paro improved healing, compared to an inactive control group. Listening to music did not influence healing, but significantly increased stimulation. The effects of enrichment on healing were mediated by enjoyment. A small randomised pilot study was then conducted to explore effects of Paro on skin outcomes in psoriasis patients. Findings indicated feasibility issues regarding recruitment, yet moderate effect sizes showed some promise.

In theme two, a pilot study examined the effects of viewing landscapes, compared to scrambled versions of these artworks, on recovery from a stressor. Viewing landscapes did not reduce stress, but instead increased psychological and physiological stimulation, compared to viewing scrambled artworks. To investigate these effects further, a scoping review was conducted on the effects of viewing artworks on stress. The 14 included studies demonstrated a lack of homologous and rigorous research. However, preliminary results demonstrated reliable decreases in self-reported stress and systolic blood pressure. Moderating factors may explain the divergent effects observed.

Overall, the thesis demonstrated that social enrichment (Paro) increased enjoyment and improved skin healing in a healthy stressed population. Other forms of sensory enrichment (music and artwork), increased stimulation, rather than reducing stress, and did not affect healing. These findings suggest that different forms of environmental enrichment may affect health via different pathways in humans. Future research should further investigate the implications of these findings clinically, and explore moderating variables.

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I would like to extend a massive thank you to everyone that has helped me and provided me with support over this PhD candidature. You do not understand how much your support has helped me.

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List of Abbreviations

ART	Attention restoration theory
AVI	Affect valuation index
BMI	Body mass index
BP	Blood pressure
EE	Environmental enrichment
HA	High arousal
HAN	High arousal negative affect
HAP	High arousal positive affect
HPA	Hypothalamic-pituitary-adrenal
HR	Heart rate
HRV	Heart rate variability
IL	Interleukin
LA	Low arousal
LAN	Low arousal negative affect
LAP	Low arousal positive affect
NA	Negative affect
PA	Positive affect
PANAS	Positive and negative affect schedule
PASI	Psoriasis area and severity index
PC	Principal component
PCA	Principal component analysis
PHQ-9	Patient Health Questionnaire-9
PNS	Parasympathetic nervous system
PRISMA-ScR	Preferred reporting items for systematic reviews and meta-analyses extension for scoping review
PSS	Perceived stress scale
sAA	Salivary alpha-amylase

SAM	Sympathetic adrenal medullary
SBR	Skin barrier recovery
sCort	Salivary cortisol
SNS	Sympathetic nervous system
TEWL	Trans-epidermal water loss
TNF-α	Tumour necrosis factor alpha
TSST	Trier social stress test

Publisher Approvals

1. **Chapter 3-** Law, M., Jarrett, P., Nater, U. M., Skoluda, N., & Broadbent, E. (2020). The effects of environmental enrichment on skin barrier recovery in humans: A randomised trial. *Scientific Reports*, 10(1), 1-11. https://doi.org/10.1038/s41598-020-66687-2. Published by Nature Research, Springer Nature. Manuscript is open access and made available for re-use under the Creative Commons Attribution (CC-BY) license. Appears on pages 28-51.

2. **Chapter 4-** Law, M., Jarrett, P., Nater, U. M., Skoluda, N., & Broadbent, E. (2020). The effects of sensory enrichment after a laboratory stressor on human skin barrier recovery in a randomized trial. *Psychosomatic Medicine*. https://doi.org/10.1097/PSY.0000000000000858**.** Published by Lippincott Williams & Wilkins. Permission to reuse obtained 22/09/2020. This is a non-final version of an article published in final form in *Psychosomatic Medicine.* Appears on pages 54-77.

3. **Chapter 5**- Law, M., Jarrett, P., Nieuwoudt, M. K., Holtkamp, H., Giglio, C., & Broadbent, E. (in submission). The effects of Paro robot in patients with psoriasis: A pilot study. Appears on pages 81-103.

4. **Chapter 6-** Law, M., Minissale, G., Lambert, A., Nater, U. M., Skoluda, N., Ryckman, N., Tahara-Eckl, L., Bandzo, M., & Broadbent, E. (2020). Viewing landscapes is more stimulating than scrambled images after a stressor: A cross-disciplinary approach. *Frontiers in Psychology*, 10, 3092. https://doi.org/10.3389/fpsyg.2019.03092. Published by Frontiers Media. Manuscript is open access and made available for re-use under the Creative Commons Attribution (CC-BY 3.0) license. Appears on pages 106-125.

5. **Chapter 7**- Law, M., Karulkar, N., & Broadbent, E. (in submission). Evidence for the effects of viewing visual artworks on stress outcomes: A scoping review. Appears on pages 128-151.

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Extent of contribution by PhD candidate (%)	90

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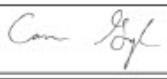
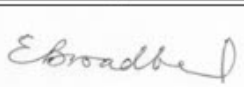
Cannon Giglio		21 Oct 2020
Elizabeth Broadbent		20/10/2020

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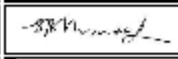
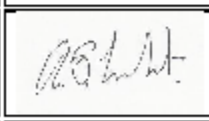
Gregory Minissale		5 June 2020
Anthony Lambert		5 June 2020
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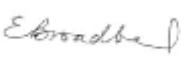
Elizabeth Broadbent		29/07/20

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Extent of contribution by PhD candidate (%)	70%

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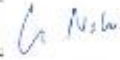
Urs M. Nater		05.06.2020
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Nature of contribution by PhD candidate	Development of review protocol, completed search strategy, screening, data extraction, and writing and submission of the manuscript.
Extent of contribution by PhD candidate (%)	95

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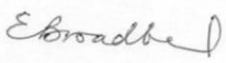
Elizabeth Broadbent		20/10/2020

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Chapter 1- Overview

1.1 Introduction to Thesis Topic

Environmental enrichment (EE) refers to a manipulation in which the physical and social environment of an organism is altered and enhanced to promote and facilitate sensory, social, cognitive and physical stimulation (Girbovan & Plamondon, 2013; Janssen et al., 2012; Khan et al., 2016). The concept of EE arose in the 1940's when Donald Hebb found that his rats performed better on learning and problem-solving tasks when they were raised as pets and free to roam his house, compared to rats raised in a laboratory environment (Hebb, 1947). This incidental finding developed the awareness that environmental impoverishment could be detrimental to animals. Since then, research into enriching captive animals' environments has flourished. EE can therefore be understood as a continuum from an enriched to an impoverished environment.

In this research area, EE generally refers to the modification of a captive animal's housing environment to improve the animal's welfare above 'standard' housing (Singhal et al., 2014); but it has also been used to refer to enriching the human environment (Janssen et al., 2012). The enriched environment can therefore range from an experimental approach in animals, to an active physical, social and mental lifestyle in humans (De la Fuente & Arranz, 2012).

There is a myriad of ways to provide enrichment and this differs between humans and animals, as well as between and within animal species (Crofton et al., 2015). Taxonomically, EE has been subdivided into multiple categorisations that can be employed either individually or as a multifaceted enrichment strategy. These include: social enrichment (e.g. social support or social housing), sensory enrichment (e.g. tactile, auditory,

or visual facilitation), cognitive enrichment (e.g. puzzles or cognitive training) and motor enrichment (e.g. exercise) (Clemenson et al., 2015; Janssen et al., 2012; Singhal et al., 2014). Animal studies also classify food as a form of enrichment; however, there has been controversy with this categorisation due to the confounding effects of nutrients (Singhal et al., 2014). The type of enrichment chosen can affect outcome variables differently, so careful consideration of the appropriate type is important (de Azevedo et al., 2007).

Among these different types of EE, common characteristics include: novelty, choice, controllability, unpredictability and complexity (Girbovan & Plamondon, 2013; Sampedro-Piquero & Begega, 2016). These factors provide a range of opportunities to engage in activity and stimulation. Programs can range from small environmental changes, such as the addition of toys or a running wheel to a rat's cage, to complex plans involving time-dependent rotations and combinations of different types of enrichment items (Schapiro, 2002). EE therefore provides animals or humans opportunities to experience a variety of sensory, cognitive, physical and social inputs in order to maintain a mentally and physically active lifestyle.

Extensive research has been conducted investigating the effects of EE on psychological and physiological health in animals. For example, in animal studies EE has been found to improve cognitive functioning (Kotloski & Sutula, 2015), improve learning and memory (Dolivo & Taborsky, 2017), decrease anxiety and depressive symptoms (Nawaz et al., 2017; Novaes et al., 2017), protect against neurodegenerative disorders (Faherty et al., 2005), improve immune cell function (Arranz et al., 2010; Brod et al., 2017), decrease pain (Pham et al., 2010), and reduce stress (Belz et al., 2003; Moncek et al., 2004; Ragu Varman et al., 2012). However, while there is substantial research demonstrating the beneficial effects of EE in animals, little research has been conducted in human samples.

1.2 Research Aims

The broad aim of this thesis was to experimentally investigate whether the effects of EE found in animal research can translate to human populations. More specifically, this thesis is investigating the effectiveness of various sensory EE interventions (including a Paro robot, music, comfort items and artwork) on improving stress and wound healing outcomes in human participants, including a clinical sample with psoriasis. Paro also provides a form of social enrichment as it looks and acts like a baby seal. This thesis aims to use the knowledge gained from four experimental studies and a scoping review to add to the knowledge base on how best to use EE to improve clinical outcomes in humans.

1.3 Thesis Outline

To investigate the above aims, Chapter 2 begins by establishing a theoretical overview of the literature relating to the effects of stress on health and wound healing, and in particular how EE could be a possible intervention to reverse these negative effects. The topic of stress and wound healing was chosen because stress has been reliably shown to impact hormones, the function of the immune system, and wound healing processes. This provides a sound model in which to study the effects of EE on both psychological and physiological processes. Chapter 2therefore overviews the research of EE on stress and wound healing in both animal and human studies, before discussing the enrichment interventions used within this thesis.

The subsequent chapters present four experimental studies and one scoping review completed as part of this thesis. These chapters can be considered as two themes. The first theme includes Chapters 2, 3 and 4 which report three experimental studies investigating the effects of different EE interventions on skin healing and stress. The second theme includes

an experimental pilot study and a scoping review examining the effects of visual EE, in the form of viewing artworks, on stress outcomes.

Chapter 3 presents the manuscript of the first experimental study investigating the effects of three types of sensory EE on wound healing in humans (Study 1; Law, Jarrett et al., 2020a). In this study, participants underwent a standardized tape-stripping procedure to remove the top layer of the epidermis, the stratum corneum. Participants were randomized to interact for 30 minutes with one of three EE interventions (comfort items, a Paro robot or music) or a control group, to investigate whether any of these types of EE could improve skin barrier recovery (SBR) rates. Although the conditions had different levels of stimulation and relaxation after the interventions, there were no differences in SBR between any of the conditions. Possible methodological reasons for this lack of effect are discussed, including the fact the sample was not stressed and the use of an active control group.

Chapter 4 then presents the manuscript of a second experimental study which aimed to address some of the methodological limitations from Study 1 (Study 2; Law, Jarrett et al., 2020b). This study followed a similar method to Study 1, however, an experimental stressor was introduced after the tape-stripping procedure to ensure the sample was sufficiently stressed to experience the stress-reducing effects of EE. Also, an inactive control condition was used to remove possible confounding effects. Interacting with the Paro robot after the stressor was found to lead to significantly improved SBR rates, compared to the control condition. This effect was found to be mediated by participants' levels of enjoyment, therefore implicating a possible mechanism for this effect.

Chapter 5 presents the manuscript of a third experimental study, which follows on from the results of Study 2, and extends the research to a patient sample (Study 3). This study aimed to investigate the effects of interacting with the Paro robot after a stressor in patients

with psoriasis, a skin disorder known for its links to psychological stress and the immune system. Unfortunately, due to recruitment issues and COVID-19 restrictions, only 25 patients with psoriasis could be recruited and therefore, the study was not powered to detect significant effects between the Paro and control conditions. However, changes in psychological and skin outcomes were found across the experimental session, indicating the feasibility of the experimental procedure for future research with a larger sample.

In the second theme of this thesis, Chapters 6 and 7 report on the effects of viewing artworks on stress. Chapter 6 begins by presenting a manuscript of a pilot study investigating the effects of viewing landscape artworks (compared to scrambled versions of the images) on the psychological and physiological recovery from a laboratory stressor (Study 4; Law, Minissale et al., 2020). Findings from this study demonstrated that viewing landscape artworks was more stimulating than viewing scrambled artworks.

The fifth manuscript from this thesis is included in Chapter 7, which is a scoping review on the effects of viewing artworks on stress outcomes. This scoping review found a lack of high-quality research in this area with high heterogeneity, making it difficult to compare studies and make strong conclusions. The evidence to date demonstrates that viewing artworks shows consistent reductions in self-reported stress, but has mixed effects on physiology. Gaps in the research that need to be addressed before strong conclusions can be made are identified and discussed to help direct future research in this area.

To conclude, Chapter 8 summarises the key findings from all five manuscripts and discusses these in context of existing literature. The theoretical and clinical implications of the findings from these studies are discussed. The limitations of the presented research and directions for future research are also examined.

Chapter 2- Background: Stress, Wound Healing and EE

This chapter outlines the background for the effects of stress on wound healing and in contrast, how EE may be able to counteract these negative effects. The chapter begins by describing the physiological stress response and how this can negatively affect health, with particular focus on the outcome of wound healing. EE is then proposed as a possible psychological intervention to reduce stress and improve wound healing. Evidence from animal and human research is provided to support this proposition, before the current research is discussed.

2.1 The Physiological Stress Response

Psychological stress arises when an individual perceives that the demands of the environment exceed their own capacity and resources to cope (Lazarus & Folkman, 1984). Stress is therefore comprised of three components: the stimulus in the environment (stressor) that precipitates a reaction in the brain (stress perception), and ultimately activates a physiological response in the body (stress response) (Dhabhar, 2019). This definition of stress emphasises the importance of the individual's perception of the stressor; what may be perceived as stressful for one person, may not be stressful for another. The stress response is multifaceted and activates a cascade of psychological, physiological, behavioural, immunological and biochemical changes to help the person cope with the stressor at hand.

Biochemically, stress activates the sympathetic nervous system (SNS), which is associated with energy mobilisation and the fight-or-flight response. The SNS operates through the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic adrenal medullary (SAM) system to release hormones and neurotransmitters to enable the body to respond to the

perceived challenge. These two systems interact closely with the immune system and organs in the body, including the skin.

When a stressor is perceived, the SAM system releases the catecholamines epinephrine (adrenalin) and norepinephrine (noradrenalin) into the bloodstream from the adrenal medulla (Gunnar & Quevedo, 2007). These catecholamines quickly prepare the body for the fight-or-flight response by increasing heart rate (HR), respiration and blood pressure (BP), and by inhibiting digestion, urination and salivation (O'Connor et al., 2020). The effects of epinephrine and norepinephrine are quick acting as they directly innervate the body's organs including the lungs, heart, skeletal muscles, kidneys and gut (Charmandari et al., 2005). This allows for the quick response of the body to the stressor.

On the other hand, the HPA axis is responsible for the endocrine stress response, and activation leads to increased serum concentrations of adrenocorticotropic hormone released by the anterior pituitary gland and glucocorticoids (cortisol in humans and corticosterone in rodents), released by the adrenal cortex. These hormones act to release energy for use by the brain and skeletal muscles, and alter the inflammatory response to prepare the body to resist the stressor. Glucocorticoids can modulate a range of immune functions including cytokine expression and immune cell trafficking, thereby influencing the immune response (Vileikyte, 2007).

Salivary alpha-amylase (sAA) and salivary cortisol (sCort) are important biomarkers of the SAM system and HPA axis respectively (Skoluda et al., 2015). The HPA axis is slower and more sustained than the SAM system, with cortisol taking 25 minutes to peak in the bloodstream, whereas epinephrine enters the bloodstream almost immediately (Gunnar & Quevedo, 2007). Therefore, the effects of cortisol have a longer latency, but continue for long periods, even after the stressor has subsided.

On the other hand, the parasympathetic nervous system (PNS) works in opposing function to the SNS and is associated with restorative functions such as rest and recovery. The PNS therefore controls the activities of the body under normal, non-stressful conditions (Thayer et al., 2009). As well as this, the PNS can withdraw the HPA axis and SAM systems to restore the body back to normal after a stressor has ceased (Charmandari et al., 2005). In this way, the PNS decreases HR, BP and respiration, and promotes normal physiological functions such as digestion, that are blunted by the SNS (McEwen, 2008). Therefore, the SNS and PNS work in tandem to control the physiological response to a stressor.

Although commonly reported as a negative process, these stress systems are adaptive for humans. The HPA axis and SAM systems are elicited in order to deal with the demands and/or threat at hand to promote survival during the fight-or-flight response. Stress hormones allow energy to become available and be redirected around the body, particularly to the muscles and brain for immediate use to deal with the threat (Schneiderman et al., 2005). The immune system is also activated by acute stress to prepare for possible injury or infection (Dhabhar, 2019). On the other hand, less critical activities, such as digestion, growth and sexual activity, are suspended to allow for a primary focus on the threat at hand. The acute stress response is therefore evolutionarily adaptative for fight-or-flight function in the face of a threat to improve chance of survival. However, chronic activation of either of these stress systems can lead to impaired physiological functioning, including chronic immunosuppression.

2.2 Stress and Health

Under normal conditions, the PNS acts to control glucocorticoid and catecholamine release by a negative feedback system to prevent the over-activation of the HPA axis and SAM system (O'Connor et al., 2020; Padgett & Glaser, 2003). Using this system,

glucocorticoid and catecholamine secretion is inhibited when circulating levels become too high. This promotes adaptation in response to acute threatening situations and is generally beneficial for health.

However, chronic stress can suppress this negative feedback, leading to chronic activation of these stress systems and therefore elevated hormone levels in the body (O'Connor et al., 2020). This chronic activation can be detrimental to health over time, especially in older or unhealthy individuals, as the body remains in a constant state of alert. This constant pressure on physiological systems can lead to wear and tear and an inability to maintain normal physiological functioning (Rousset & Halioua, 2018). This can result in direct physical manifestations of stress in the body. For example, although increases in BP and HR are beneficial during acute stress to respond to a stressful event or threat, sustained increases in BP and HR can lead to damage to the cardiovascular system. Over time, this can result in increased chances of cardiovascular disease, stroke and heart attacks due to damaged arteries and plaque formation (McEwen, 2008; Schneiderman et al., 2005). Similar wear and tear can also occur to other physiological systems in the body including the immune and neuroendocrine systems.

There are many human studies that demonstrate the link between chronic stress and impaired physical health. For example, early studies found that chronic stress can suppress the immune system and therefore lead to higher susceptibility to diseases, such as the common cold (Cohen & Williamson, 1991). More recent meta-analyses and reviews have demonstrated that chronic stress can have strong and direct negative influences on many measures of physical health including; general health (Yu et al., 2007), cardiovascular disease and stroke (Kivimäki & Steptoe, 2018), HIV/AIDS and cancer progression (Cohen et al., 2007) and immune responses to infections and vaccinations (O'Connor et al., 2020).

Therefore, chronic stress is detrimental to one's health as stress can elicit long-term disturbances in the body, which can lead to impaired physical health.

Stress can also have negative impacts on psychological health. Activation of the stress response can lead to an increase in negative emotions, such as anxiety, anger or sadness, which if experienced long-term, can impact a person's mental health. For example, chronic stress can increase the occurrence of anxiety and depression symptoms and disorders (McEwen, 2008; Morris et al., 2010), as well as trigger schizophrenia (Corcoran et al., 2003) and bipolar disorder (Johnson & Roberts, 1995). The prolonged pro-inflammatory response of the stress systems can also have more direct effects on psychological health, including activating sickness behaviours and depression (Schneiderman et al., 2005). Therefore, chronic stress is detrimental to both physiological and psychological health.

2.3 Wound Healing

Wound healing is a sequence of events that restores and repairs tissue back to near normal function and structure after an injury (Tortora & Derrickson, 2018). The ability of the skin to heal wounds quickly and efficiently is indicative of good health and immune function (Christian et al., 2006). Wound healing involves a complicated cascade of physiological events that can be influenced by a person's psychological state. Wound healing is an important outcome to investigate the effects of stress on the body, as research consistently demonstrates that stress can impair wound healing rates. Wound healing can therefore act as a model to represent how stress can affect the physiological processes of the body (Robles et al., 2009).

Wound healing research is clinically relevant, as it can be applicable for people with chronic or acute wounds. In particular, wound healing is a critical outcome for surgery patients. Poor wound healing in surgical patients can lead to infections, scarring,

complications and longer hospital stays (Broadbent et al., 2003; Geers et al., 2018). Poor wound healing can thus affect the patient's quality of life, morbidity and mortality, as well as lead to increased healthcare costs and demand on the healthcare system (Eming & Tomic-Canic, 2017). Non-healing wounds are particularly pertinent in populations who are at-risk of poor healing due to lowered immune function, such as older adults (Guo & DiPietro, 2010). Therefore, interventions aimed at improving wound healing are important to research to minimise these clinical effects of poor healing.

2.3.1 Stages of Wound Healing

When an injury occurs, and tissue is damaged, wound healing progresses through several interdependent and overlapping stages involving the interaction of different immune cells. These stages include: haemostasis, inflammation, proliferation and remodelling (Kirwan & Pignataro, 2016; Walburn et al., 2009).

The initial stage is characterised by haemostasis and vasoconstriction to prevent excessive blood loss (Velnar et al., 2009; Walburn et al., 2009). A provisional wound matrix is formed by the fibrin blood clot to provide a scaffold for the migration of cells in the subsequent stages of healing (Reinke & Sorg, 2012). This stage occurs immediately after the injury and is usually completed after a few hours.

This stage is then followed by the inflammatory stage, which aims to establish an immune barrier against infection and remove foreign matter and dying cells to prepare the wound for healing (Tortora & Derrickson, 2018). This stage is dominated by the recruitment of neutrophils and macrophages to the wound site to kill bacteria and debride the necrotic tissue via phagocytosis (Velnar et al., 2009). At this stage, proinflammatory cytokines, including interleukins (IL) and tumour necrosis factor alpha (TNF-α) are present in the wound site to protect against infection and prepare the tissue for repair by recruiting and activating further

phagocytic cells to the wound (Christian et al., 2006). This stage begins a few hours post-injury and peaks one to three days later.

After a few days, the proliferation stage begins to shift the healing from an immune response towards tissue repair. Keratinocytes, fibroblasts, and endothelial cells migrate to the wound site to begin re-vascularisation and tissue regeneration by generating granulation tissue (Christian et al., 2006; Walburn et al., 2009). The fibroblasts also help wound contraction, allowing the wound edges to approximate together. The synthesis of collagen begins the scar response and the formation of an extracellular matrix which replaces the provisional matrix provided by the fibrin clot (Ebrecht et al., 2004; Gidron, 2019).

Remodelling is the final stage in the wound healing process and is responsible for the development of a new epithelium and scar formation (Velnar et al., 2009). While immune cell numbers and wound metabolic activity decrease, collagen deposition increases to form scar tissue. The repaired scar tissue is not identical to the original skin but is functionally and structurally intact. This stage may continue for weeks or months (Gouin & Kiecolt-Glaser, 2011).

Wound healing therefore involves a cascade of cellular and biochemical events where any problems or delays in one of the earlier stages can have implications for successive stages and therefore overall healing. A fully functioning immune system is therefore needed for successful healing. Wounds are classified as acute if they progress through these stages at a predictable and appropriate rate (Walburn et al., 2009). However, if any of the stages are compromised, wound healing can be delayed and the wound can become a chronic and non-healing.

2.3.2 The Effects of Stress on Wound Healing

There is substantial evidence that the stages of wound healing described above can be impaired by psychological factors, including stress. One meta-analysis showed that various forms of stress impaired healing in a variety of settings with an overall moderate effect size (Walburn et al., 2009). This has been found in both experimental and natural wounds, as well as with both experimental and naturally induced stress. For example, Kiecolt-Glaser and colleagues (1995) found that caregivers of Alzheimer's patients (a chronic stressor) took 24% longer to heal from an experimental punch biopsy wound than controls. Other studies have also demonstrated that stress delays SBR after an experimental tape-stripping wound, which removes the epidermis (Altemus et al., 2001; Fukuda et al., 2015; Garg et al., 2001; Robles, 2007). These studies therefore demonstrate a role of psychological stress in delaying the wound healing process.

The mechanisms behind how and when stress delays wound healing are complex and not yet fully understood. However, research has demonstrated that the stress response can affect the concentrations of immune cells important for successful wound healing. As discussed above, stress activates the HPA axis and SAM system causing an elevation in epinephrine, norepinephrine, and cortisol. Although these hormones are important to the wound healing process, when chronically activated they can suppress the secretion of pro-inflammatory cytokines, including ILs and TNF-α, which are crucial to wound healing (Glaser & Kiecolt-Glaser, 2005; Segerstrom & Miller, 2004). Chronic stress can therefore cause an immunosuppressive effect at the early inflammatory stage of wound healing, delaying the subsequent stages of healing (Christian et al., 2006).

Excessive cortisol has also been shown to reduce macrophage and neutrophil concentrations, therefore decreasing phagocytosis in the wound which can increase chance of infection (Koschwanez et al., 2015; Rojas et al., 2002). Lastly, increased concentrations of

epinephrine and norepinephrine from the SAM system have been shown to inhibit fibroblast growth, which impedes the proliferation stage of wound healing and delays wound closure (Maarouf et al., 2019). Therefore, chronic psychological stress can directly influence multiple types of immune cells and therefore delay wound healing at different stages.

Under acute stress, the HPA axis can regulate the increases in cortisol via a negative feedback system to minimise negative effects on health (Chen & Lyga, 2014). Cortisol is important for the immune response and does not negatively impact wound healing until it raises beyond typical basal concentrations (DeVries et al., 2007). Acute stress and acute increases in cortisol can actually be immunoenhancing as they lead to the activation of the immune system and a significant redistribution and migration of immune cells from the blood to the skin (Dhabhar, 2000; Schneiderman et al., 2005). This includes increasing the numbers, circulation and function of leukocytes, macrophages, neutrophils, lymphocytes and natural killer cells in the skin; immune cells which are beneficial to the wound healing process (Dhabhar, 2014; Schneiderman et al., 2005). This can therefore lead to enhanced wound healing and successful stress adaption in acute situations. However, even a modest increase in stress can overwhelm this system and compromise the wound healing process, leading to the suppression and dysregulation of the immune system and therefore impaired wound healing.

As well as the direct physiological effects of stress on wound healing, stress can lead to damaging health behaviours that indirectly influence wound healing rates. For example, stress can increase alcohol consumption, smoking, unhealthy eating, sleep disturbances and sedentary behaviour, all of which can compromise the different stages of wound healing (Glaser & Kiecolt-Glaser, 2005).

The effects of stress on wound healing are significant enough to have health implications for patients. Even a minor delay in wound healing due to stress can lead to increased chance

of infection and complications, lengthened hospital stays and increased healthcare costs. Therefore, the effects of psychological stress on wound healing are clinically relevant and this highlights the importance of reducing stress levels in wounded patients.

2.3.3 Psychological Interventions for Wound Healing

Since stress impairs wound healing, psychological interventions to reduce stress should be able to counteract these effects and improve healing. Systematic reviews by Robinson, Norton and colleagues (2017) and Geers and colleagues (2018) demonstrate there is mounting evidence that psychological interventions have positive effects on wound healing. This has been shown with a variety of different interventions including; expressive writing (Koschwanez et al., 2013; Robinson, Jarrett et al., 2017; Weinman et al., 2008), relaxation (Broadbent et al., 2012; Robinson, Jarrett et al., 2015), social support (Robinson, Ravikulan et al., 2017), hypnosis (Ginandes et al., 2003) and mindfulness-based stress reduction (Meesters et al., 2018).

These interventions may work in opposition to stress to reduce HPA axis and SAM system activity and up-regulate the immune system, which may therefore translate to improved wound healing. These interventions may also promote more adaptive coping behaviours that have indirect effects on healing. Many of these interventions are low-cost, feasible and have few, if any, side-effects, making them easy to implement. Stress-reducing psychological interventions could therefore have important implications for clinical and surgical wounds. However, these interventions may only be effective in people already experiencing stress-related immune dysregulation and may have little effects in non-stressed individuals.

2.4 EE as an Intervention to Improve Stress and Wound Healing

More research is needed on whether different kinds of psychological interventions can improve both stress and wound healing and the mechanisms involved. EE has been proposed

to normalise HPA and SAM activity and improve the immune response (Coleman et al., 2013; Fricchione & Levine, 2017) and therefore, EE could be a further psychological intervention to improve stress and wound healing. However, there is little research examining the effects of EE paradigms on stress and wound healing in human populations.

2.4.1 EE and the Stress Response in Animals

There is substantial evidence that EE can influence the stress response in animals. In particular, most evidence demonstrates that EE is associated with the dampening down of the physiological stress response and this therefore counteracts the negative effects of stress on health. For example, after a stressor EE housing (including the addition of toys, running wheels and mazes) has been shown to: decrease stress behaviours and increase play behaviours in rats (Klein et al., 1994; Morley-Fletcher et al., 2003), prevent the emergence of anxiety and depression symptoms in rats (Nawaz et al., 2017; Novaes et al., 2017; Seong et al., 2017), and reverse the negative effects of stress on HR and cardiovascular function in voles (Normann et al., 2018) and on hippocampal memory and learning in rats (Wright & Conrad, 2008). These studies indicate that long-term EE leads to a lower reactivity to stress.

However, despite the proposition that EE is stress-reducing, there have been some inconsistencies in the literature about precisely how EE affects stress, especially in regards to the hormonal stress response (Fairhurst et al., 2011). EE has been found to increase (Benaroya-Milshtein et al., 2004; Moncek et al., 2004), decrease (Belz et al., 2003; Mesa-Gresa et al., 2016) and have no effect on (Dandi et al., 2018; Schrijver et al., 2002) baseline corticosterone levels in different studies. However, these studies are difficult to directly compare as they use different procedures, types and durations of EE.

Generally, the evidence indicates that EE increases corticosterone levels short-term, therefore signifying an increase in stimulation and the stress response. However, further

evidence demonstrates that long-term EE leads to decreases in corticosterone to below baseline levels, blunted corticosterone increases in response to stress and faster return to baseline after stress, compared to rodents in standard housing (Belz et al., 2003; Moncek et al., 2004; Morley-Fletcher et al., 2003; Ragu Varman et al., 2012). These findings have especially been obtained in studies of rodents who have been exposed to early life stress such as social isolation. In these rodents, EE can buffer the detrimental effects of early life stress on the rodents' stress response and return the levels of stress hormones back to baseline levels (Coleman et al., 2013). Therefore, long-term EE leads to a more adaptive HPA axis and more efficient corticosterone response to stress.

In light of these findings, Crofton and colleagues (2015) propose an inoculation stress hypothesis of EE in rodents. This hypothesis states that mild chronic stress (or eustress) from living in an enriched environment can inoculate animals against subsequent stressors by suppressing the immune response to stress. In this way, animals exposed to an enriched environment become resilient to future stressors through exposure. This results in a decrease of the negative health effects usually caused by chronic stress. This hypothesis can therefore explain why short-term and long-term EE may have different effects on corticosterone levels.

2.4.2 EE and the Immune Response in Animals

EE has been found to affect immune functioning in animals in ways that may influence healing. In rodents, long-term enriched housing has been shown to alter the levels of immune cell markers including; pro-inflammatory cytokines (Arranz et al., 2010; Giovanni Laviola et al., 2004; Nachat-Kappes et al., 2012) and neutrophils (Brod et al., 2017). Research has also demonstrated that EE can improve immune cell function including; macrophage chemotaxis, phagocytosis, proliferation and natural killer cell activity (Arranz et al., 2010; Benaroya-Milshtein et al., 2004), enhance inflammation and infection responses (Brod et al., 2017),

improve macrophage and natural killer cell activation (Garofalo et al., 2015), and increase T-cell infiltration (de Sousa et al., 2011).

Lastly, the effects of EE on immune function can been seen through clinical outcomes in animals. For example, long-term enrichment in mice can lead to increased immune response and antibodies to vaccinations (Benaroya-Milshtein et al., 2007; Gurfein et al., 2014), faster virus clearance (de Sousa et al., 2011), fewer negative effects from the influenza infection (Jurgens & Johnson, 2012), and decreased tumour size and growth (Garofalo et al., 2015; Nachat-Kappes et al., 2012). Therefore, there is substantial evidence to suggest that EE can affect the immune response in animals. This indicates that EE may also be able to affect wound healing.

2.4.3 EE and Wound Healing in Animals

Unlike the evidence for stress and immunity, the evidence for the effects of EE on wound healing in animals is limited. One important study in this area examined the effects of tactile enrichment on wound healing in rodents. Vitalo and colleagues (2009) found that isolation reared rats provided with EE in the form of nestlets (nest building material) for four weeks had significantly faster wound healing when compared to isolation reared rats without the nestlets. Even more importantly, the isolation reared rats provided with EE and group reared rats showed no significant difference in wound healing rates. This indicates that the nestlets reduced the negative effects of isolation on healing.

A further experiment demonstrated that the EE provided through nestlets improved healing to a similar degree as the provision of oxytocin, suggesting a possible mechanism behind these effects (Vitalo et al., 2009). Oxytocin is a hormone that is released during social contact and is associated with social bonding (Detillion et al., 2004). Exogenous oxytocin appears to suppress the stress response and buffer the deleterious effects of stress on wound

healing (Detillion et al., 2004). The fact that oxytocin caused a similar improvement in wound healing to the nestlets suggests that this form of EE may improve wound healing through a similar mechanism to social enrichment. The nestlets promote nest building behaviour, which is a key social bonding activity for rodents and their offspring.

Other research has found that EE can enhance tumour wound repair processes in mice, resulting in improved survival (Bice et al., 2017). These improvements occurred due to enhanced revascularisation and immune cell recruitment and secretion. Therefore, there is some evidence to demonstrate that EE may be able to improve wound healing rates in animal studies; however, more research is needed to further support this evidence base.

2.4.4 Evidence for the effects of EE in Humans

The evidence above demonstrates that EE has been extensively researched within animal samples. However, there is limited evidence if these effects translate clinically to human populations. There are many issues with attempting to translate the animal research to humans, and these issues are described in the introduction of Chapter 3. Despite these issues, there is some evidence to suggest that the effects of EE in humans may be similar to the effects of EE in animals.

Although humans tend to already live in an enriched environment, further opportunities for enrichment can still be provided. EE in humans can occur within all types of enrichment. For example, social enrichment can include social support or activities that involve social interaction; cognitive enrichment can include puzzles, cognitive training and education; motor enrichment can include items and environments that promote exercise; and lastly sensory enrichment can include anything that stimulates the senses such as music, artwork or different textures (Singhal et al., 2014).

Similar to animal research, it is important for human EE to include novelty, choice, controllability, unpredictability and complexity. EE interventions in humans provide opportunities for enrichment, and the person makes the choice whether to engage. These factors are especially important for humans over animals because humans have extra inter-personal factors that affect their engagement with EE. For example, humans have the extra factor of motivation; we must be motivated to choose to engage with the EE (Frasca et al., 2013). This may be affected by personality characteristics and early life experiences leading to different degrees of motivation and acceptability for different types of EE. What might be enriching for one person, may not be for another, and this motivation may also fluctuate throughout life (Queen et al., 2020; J. H. White et al., 2015). Therefore, these individual differences may make translating animal EE to humans even more difficult and highlights the importance of personalising EE interventions for different individuals.

Although not often operationally defined as EE, we can see many examples of EE in clinical settings. For example, in hospitals that are known to be sensorially deprived, the provision of stimulating equipment (such as games, books, music, magazines, art and puzzles) may provide EE and therefore reduce stress and improve healing (Rosbergen et al., 2017; J. H. White et al., 2015). Research has particularly focussed on the addition of EE to stroke units. These studies have found that the provision of EE in the form of reading materials, computers, music, puzzles, games and artistic activities, can lead to shorter hospital stays, increased activity levels, lower depression, stress and anxiety, and increased cognitive functioning (Janssen et al., 2014; Khan et al., 2016; Rosbergen et al., 2017; J. H. White et al., 2015). This has large implications for recovery, as patients who are more active, tend to recover quicker (McDonald et al., 2018). These outcomes were also found to be maintained at three months follow up, demonstrating the possible long-term impacts of EE in humans (Khan et al., 2016).

Retirement homes are another example of an impoverished environment, where the provision of EE (such as music therapy, art therapy and movement therapy) is often delivered to residents in order to engage their bodies and minds (Ross, 2017). Multi-sensory stimulation may be particularly effective in this population as retirement homes often have little sensory stimulation. In older adults, multi-sensory EE has been found to improve cognition and mood, and decrease stress, anxiety and depression, especially in those who are institutionalised and therefore live in more deprived environments (Bygren et al., 2013; De Oliveira et al., 2014; Moghaddasifar et al., 2019). Thus, hospitals and retirement homes are two examples of places where EE could be used to further enrich humans' environments; however, there are also many other clinical applications.

EE has been commonly used in targeted interventions for specific patient groups through sensory integration therapy and multi-sensory environments. In autistic children, this form of EE has been found to improve sensory, non-verbal, cognitive and motor skills (Weitlauf et al., 2017), as well as decrease autism symptoms (Aronoff et al., 2016; Woo & Leon, 2013). Similar effects are seen for patients with traumatic brain injuries, with one scoping review demonstrating that the provision of EE can improve long-term outcomes including lessening cognitive decline and improving cognitive functioning (Frasca et al., 2013). Lastly, multi-sensory stimulation is used in patients with dementia to increase alertness and cognitive functioning, reduce behavioural problems and agitation, and improve quality of life (Jakob & Collier, 2017; Strøm et al., 2016; Vozzella, 2007). However, these clinical patient studies tend to have small sample sizes and limited follow-up, so it is difficult to make strong conclusions about the efficacy of EE in these populations.

More recently, EE in humans can include technological approaches including the use of virtual reality, tablets and computers to provide enrichment opportunities (Rosbergen et al., 2016). This can include cognitive stimulation through games or puzzles, auditory stimulation

through music or nature sounds, visual stimulation through viewing art, videos or nature, and social interaction, through video calls and instant messaging. For example, playing complex 3D video games can result in improved memory and cognitive performance, especially for older adults to whom these games are novel and unique (Clemenson & Stark, 2015; Clemenson et al., 2020). Virtual reality has also been used in various studies with both older adults and the general public to demonstrate that the effects of EE on cognition, relaxation and stress can also be replicated from a virtually enriched environment (Repetto et al., 2016; Serrano et al., 2016; Villani & Riva, 2012). Visual enrichment through viewing artwork or nature images on tablets, virtual reality devices or virtual windows have also been shown to reduce stress and improve wellbeing (McCabe et al., 2013; Tyack et al., 2017; M. P. White et al., 2018). Therefore, the use of technology could help to provide further EE for humans.

Lastly, EE in humans could encompass cultural or social engagement, such as attending social events, completing further education, or visiting museums, galleries, cinemas or theatres. For example, this engagement has been shown to decrease depression (Fancourt & Tymoszuk, 2018; Fancourt & Steptoe, 2019), improve mental wellbeing (Renton et al., 2012), reduce risk of mortality (Väänänen et al., 2009), improve health related quality of life (Hajek et al., 2017), and reduce incidence of depression (Fancourt et al., 2018). Thus, EE in humans can encompass more than just their direct environment, but also their larger community and the opportunities for enrichment that this community may provide.

EE can therefore be an appealing intervention as it can increase activity and stimulation in deprived patients. Often, EE interventions for humans only involves a one-off purchase of enriching items and little staff involvement (Janssen et al., 2012). Therefore, EE could be an effective non-pharmacological approach in humans to improve stress and wound healing.

2.4.4.1 EE and wound healing in humans. Although evidence from animal research provides support for the hypothesis that EE may improve healing in humans, caution must be applied since humans and animals differ vastly anatomically (Curtis & Nelson, 2003). While animal models can give a preliminary indication of what may be effective for human healing, vast differences in wound healing occur between animal species and between humans and animals, making it difficult to make conclusions without human testing (Volk & Bohling, 2013). For example, it is difficult to compare rodent and human skin healing as rodent skin is looser, thinner and more densely covered in hair than human skin, and has a layer of subcutaneous muscle, which is absent in humans (Ignacio et al., 2016). These skin dissimilarities lead to significant differences in the wound healing stages.

Despite this, there is initial evidence that EE in humans could lead to improved wound healing rates. Preliminary research suggests that some forms of social enrichment, such as social support interventions, can aid wound healing in humans, although more work is needed (Robinson, Ravikulan et al., 2017). Although auditory enrichment through music (Hole et al., 2015), and visual enrichment through artworks (Vetter et al., 2015), have been shown to improve post-operative recovery, wound healing has not been assessed as an outcome. Enriching hospital rooms has also been shown to produce positive effects including shorter hospital stays, however, again wound healing has not been directly studied (Ulrich, 1984). Therefore, more research is needed to determine if EE in humans can improve wound healing.

2.5 Current Research

The lack of research in this area makes it pertinent to conduct more studies in human populations in order to make strong conclusions about the efficacy of EE to reduce stress and improve wound healing. This thesis particularly focuses on sensory enrichment interventions.

Sensory enrichment involves items typically designed to provide stimulation to one or more of the senses (Coleman et al., 2017). Sensory enrichment can be provided in many different ways including the addition of different sounds, textures, smells and sights into the environment. In both humans and animals, sensory enrichment is less studied than the other types of enrichment, such as exercise, cognitive training and social housing. However, it is an important form of stimulation that is low-cost, non-invasive and easy to administer as it can be done by the individuals themselves, with little to no need for professional help (Singhal et al., 2014). Sensory enrichment also allows chances for multi-sensory stimulation, as a single intervention or enrichment item can stimulate multiple senses, thus improving the beneficial effects.

In the current research, four different forms of sensory enrichment were studied. All of these interventions are described in more detail in their corresponding manuscripts. Firstly, tactile enrichment, provided via soft blankets and pillows, is investigated in Study 1, reported in Chapter 3. This form of EE is investigated as it represents the human version of the nestlets provided in Vitalo and colleagues (2009) rat study. However, no research has been conducted investigating the effects of these items on stress or wound healing in humans.

Music was also studied as a form of auditory enrichment. Although there is a large existing evidence base demonstrating music's beneficial effects on stress and mood (see de Witte et al., 2019 and Finn & Fancourt, 2018 for full reviews), no research has investigated the effects of listening to music on wound healing. Music is therefore investigated as a possible EE intervention to improve wound healing in the first two studies, reported in Chapters 3 and 4.

The companion robot Paro was also investigated as a form of multi-sensory and social enrichment. Paro is a robotic seal, designed to provide companionship and entertainment

through human-robot interaction. Paro behaves proactively and also reacts to users' touch and voice by making sounds and movements, therefore providing auditory and motor enrichment. Paro is also covered in soft white fur, allowing for tactile stimulation. The social support provided by Paro could also be interpreted as social enrichment. Therefore, Paro is a stimulus which provides multi-modal enrichment. Research has shown that interacting with the Paro robot can reduce both psychological (McGlynn et al., 2016) and physiological stress, indexed through decreases in sAA (Nomura & Hoshina, 2017), BP (Robinson, MacDonald et al., 2015) and urinary stress hormones (Saito et al., 2003); however, no research has investigated healing outcomes. The effects of interacting with Paro on skin healing is therefore investigated within the first three studies, reported in Chapters 3, 4 and 5.

Lastly, artworks are investigated within this thesis as a form of visual enrichment. Research has demonstrated that viewing artworks as visual enrichment can reduce both psychological (Clow & Fredhoi, 2006; Kweon et al., 2008) and physiological (Mastandrea et al., 2019; Pearson et al., 2019) stress outcomes. However, the research in this area is heterogeneous and low quality. Therefore, the effects of viewing landscape artworks on stress is investigated in Study 4 in Chapter 6, and a broader scoping review on the effects of viewing artworks on stress is reported in Chapter 7 to direct future research in this area.

Chapter 3- The Effects of Environmental Enrichment on Skin Barrier Recovery in Humans: A Randomised Trial

3.1 Preface

As described in Chapters 1 and 2, little research has been conducted investigating the effects of EE in humans, especially on the outcome of wound healing. Therefore, the first study in this thesis explored whether three different types of sensory enrichment (music, comfort items and the Paro robot) could improve wound healing in a healthy human sample.

This study used an experimental tape-stripping procedure to create a small skin injury to examine healing over the experimental session. Tape-stripping is a procedure that removes the top-layer of skin (the stratum corneum) through the repeated application and removal of adhesive tape. As the stratum corneum is removed, an increase in trans-epidermal water loss (TEWL) is observed as water can more easily permeate the epidermis. The measurement of TEWL after the tape-stripping wound is created can be used to quantify SBR; the rate at which the epidermis has recovered from the barrier disruption. Tape-stripping is therefore a standardised procedure to quantify skin healing rates.

This procedure is a non-invasive and non-painful method to assess wound healing processes in humans over a short-time frame. The maximal healing of a tape-stripping wound occurs after only one hour and the skin barrier returns to near baseline levels after eight hours (J. C. Tsai et al., 1994). Therefore, tape-stripping is a satisfactory model of wound healing to be utilised in short-term studies, allowing for lower participant time-commitments and no need for follow up sessions. This type of wound model has been successfully used to investigate how quickly the skin can heal in many studies involving stress (Altemus et al.,

2001; Muizzuddin et al., 2003; Robles, 2007) and psychological interventions (Robinson, Jarrett et al., 2015; Robinson, Ravikulan et al., 2017).

Due to the novelty of EE research in human samples, this study used an exploratory approach to investigate multiple types of sensory EE. Accordingly, the study included three EE conditions; soft blankets and pillows as tactile enrichment, music as auditory enrichment, and the Paro robot as multi-modal enrichment. Study 1 aimed to investigate whether interaction with any of these three EE interventions over a 30-minute period could improve SBR after the tape-stripping wound. A secondary aim of this study was to investigate any possible effects of the EE interventions on both psychological and physiological stress outcomes as indexed by self-reported stress, sCort and sAA.

3.1.1 Citation

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3.2 Introduction

EE is a paradigm that involves providing sensory, cognitive and physical stimulation by altering the physical and social surroundings of the environment (Girbovan & Plamondon, 2013; Janssen et al., 2012). EE generally refers to the modification of a captive animal's environment; but it has also been used to refer to enriching human environments (Janssen et al., 2012). EE has multiple categorisations that can be employed either individually or together, including: social enrichment (e.g. social support), sensory enrichment (e.g. tactile, auditory, or visual facilitation), cognitive enrichment (e.g. brain games) and motor enrichment (e.g. exercise) (Clemenson et al., 2015; Janssen et al., 2012; Singhal et al., 2014).

Many studies in animals have investigated the effects of EE on health outcomes and generally found beneficial effects. For example, EE in rodents has been found to improve: cognitive functioning (Kotloski & Sutula, 2015), learning and memory (J. C. Bennett et al., 2006), immune function (Arranz et al., 2010; Brod et al., 2017), and both the behavioural (Klein et al., 1994; Novaes et al., 2017) and physiological (Belz et al., 2003; Moncek et al., 2004; Morley-Fletcher et al., 2003) stress responses. It has been proposed that EE has beneficial effects by attenuating the stress response (Nachat-Kappes et al., 2012), with many studies showing that enriched animals have lower corticosterone at baseline and in response to acute and chronic stress (Belz et al., 2003; Dandi et al., 2018). This reduction in stress reactivity leads to down-stream immunological and psychological benefits.

Despite substantial evidence demonstrating EE's beneficial effects in animals, few studies have been conducted in humans (McDonald et al., 2018). There are a number of issues to consider when adapting these interventions for humans. One important issue is that the definition of EE is inconsistent with no clear operationalisation. In most rodent studies, EE refers to a large cage with opportunities for exploration and the provision of novel objects including: balls, climbing structures and running wheels (Reynolds et al., 2010). However,

the objects provided vary between studies, as well as the size of the cage, the duration of EE and the degree of complexity (Ekstrand et al., 2008).

A second issue is the variable definition of the control condition, which causes further difficulties with generalisability. In many studies, a control environment is where animals are reared in simple cages with only the necessary bedding, food and water available (Sale, 2018). However, this can be seen as a state of impoverishment, with enrichment being closer to the normal state for wild animals (McDonald et al., 2018). Therefore, the provision of EE actually normalises the typical living condition and rescues the deficits caused by impoverishment. If this is true then EE may not be as effective in human populations who already live in enriched conditions.

A third issue is that animals usually have continuous access to EE over a period of weeks (McDonald et al., 2018). Such long experiments are impractical to replicate in humans because they would require isolating individuals for long periods of time. It is therefore unknown whether the effects of long-term EE in animals will translate to short-term EE in humans.

Despite these limitations, the beneficial effects in animals suggest there is merit in conducting research to examine whether EE has clinical potential for humans. Although most humans tend to already live in enriched environments, there is evidence to suggest that further enrichment can be added to human's lives (Sale, 2018). For humans, EE can include any environmental change that provides mental, physical, sensory or social stimulation (Singhal et al., 2014). Even though many human studies do not use the term EE, we can still observe EE's benefits through studies on cognitive training, sensory enhancement (e.g. art, music, movies or video games), social support, exercise and education (Clemenson et al., 2015; Sale, 2018; Singhal et al., 2014).

There are a number of applications of EE including the provision of activities to older adults in nursing homes, such as art therapy, physical exercise, social activities and brain training (De Oliveira et al., 2014). Attempts have also been made to provide EE in stroke units to enrich hospitalisation (Janssen et al., 2014; Rosbergen et al., 2017), where patients are provided with computers, reading materials, puzzles and video games. Post-stroke patients provided with EE were less likely to be inactive or asleep (Janssen et al., 2014), were more active and had fewer falls (Rosbergen et al., 2017), had improved depression, stress, and cognitive functioning scores (Khan et al., 2016).

These human studies suggest that the effects of EE seen in animals may translate to humans. However, more rigorous research is still required. The current study aims to investigate how EE could improve wound healing in humans. Wound healing is an important outcome as it is clinically relevant and can be applicable for people with chronic or acute wounds. Poor wound healing can lead to infections, complications and longer hospital stays and can affect the patient's quality of life, morbidity and mortality, as well increase healthcare costs (Eming & Tomic-Canic, 2017). Non-healing wounds are particularly pertinent in populations at-risk of poor healing due to lowered immune function, such as older adults, people with diabetes and obese individuals (Guo & DiPietro, 2010).

Fricchione and Levine (2017) propose that sensory input from the environment can facilitate wound healing. The authors state that sensory deprivation can impair wound healing, whilst the provision of EE could have the opposite effect. They theorise that this link between the environment and wound healing occurs though the 'environment-brain-skin circuit' (Fricchione & Levine, 2017). In this circuit, sensory input from the environment is processed through the sensory cortex, which in response alters HPA activity and reduces the level of cortisol in the bloodstream. This is the opposite effect that stress has on HPA axis activity, and therefore EE could buffer the detrimental effects of stress on wound healing.

In support of this theory, one study has examined the effects of tactile enrichment on wound healing in rodents. Vitalo and colleagues (2009) randomised rats into three conditions: group reared rats, isolation reared rats (a stressor) and isolation reared rats provided with nest-building material (nestlets) as a form of tactile EE. The researchers investigated the rate at which the rats recovered from a burn wound. Findings indicated that the isolation reared rats provided with nestlets had significantly faster wound healing compared to the isolation reared rats without nestlets. Even more importantly, the isolation reared rats with EE and the group reared rats showed no significant differences in wound healing, indicating the nestlets reduced the negative effects of isolation on healing. Nest building behaviour is a key aspect of social bonding, and has been shown to increase maternal behaviours, and reduce stress, possibly via central nervous system activity. The effects of providing the nestlets on wound healing were similar to the effects of administering oxytocin, a social bonding hormone. However, this research is still grounded in animal models and has yet to be tested in humans.

The primary aim of the current study was to investigate whether EE could improve wound healing in humans. As the area of EE is broad with many differing types, this research employed an exploratory approach to investigate whether different forms of sensory EE could improve wound healing, including: tactile (soft blankets), auditory (music), and a combination of social, tactile and auditory (the companion robot Paro), compared to a control condition.

The tactile condition used blankets as the human version of the nestlets used in Vitalo and colleague's study (2009). The auditory enrichment condition used music because music has been shown to decrease stress (Chafin et al., 2004; Khalfa et al., 2003) and improve immune parameters (Fancourt et al., 2014; Lu et al., 2010). The combination enrichment condition used Paro, a companion robot designed to resemble a baby harp seal and provide comfort to users. Using sensors, Paro responds to a person's touch and voice through movements and

seal noises. Paro also has a soft fur coat which provides tactile comfort when stroked. Paro therefore represents a combination of social, tactile and auditory enrichment. Preliminary studies have shown that Paro can reduce loneliness (Robinson et al., 2013), perceived stress (McGlynn et al., 2016), sAA (Nomura & Hoshina, 2017), urinary stress biomarkers (Saito et al., 2003) and BP (Robinson, MacDonald et al., 2015). No previous research has investigated any of these interventions on wound healing. The control condition was chosen as quiet reading, since this was the control condition used in previous wound healing research (Robinson, Jarrett et al., 2015; Robinson, Ravikulan et al., 2017).

The current study used a simple tape-stripping paradigm as a model of skin wound healing. This paradigm has previously been used in studies of stress and wound healing in humans, as well as an intervention study showing the provision of social support could improve healing (Robinson, Ravikulan et al., 2017). The primary outcome for this study was wound healing via SBR. Secondary outcomes included biological stress indices (sCort and sAA) as well as psychological variables.

It was hypothesised that the three EE conditions would show faster healing over the 30-minute recovery period, as shown by higher SBR, than the control condition. The EE conditions were also hypothesised to improve the psychological variables, and lower sCort and sAA compared to the control condition. No specific hypotheses were provided for differences between the EE conditions as no previous research has explored these forms of enrichment on human wound healing.

3.3 Method

3.3.1 Design

A 3 (time-point) x 4 (condition) mixed factorial experiment was performed to assess the effects of different forms of EE (control v comfort v music v Paro) on SBR after tape-stripping.

3.3.2 Sample

A sample of 120 adults (77 female, 43 male; average age 24.64 years, *SD*=7.98) was recruited from the community and university through flyers and email advertisements. Participants were included if they were over the age of 18 and spoke fluent English. Participants were excluded if they were allergic to tape, had an inflammatory dermatological condition (such as eczema or psoriasis), were taking medication that affected the immune system (e.g. systemic corticosteroids) or were pregnant. Ethics Approval was granted by the University of Auckland Human Participants Ethics Committee. All methods were performed in accordance with relevant guidelines and regulations.

3.3.2.1 Power analysis. The sample size required for an adequately powered study was calculated using the programme G*Power (Faul et al., 2007). The analysis was conducted using a linear regression model. A power level of .80 and alpha level of .05 were chosen and an expected effect size of *F*= 0.08 was estimated from a tape-stripping study on changes in SBR due to relaxation (Robinson, Jarrett et al., 2015). These parameters led to a required sample size of at least N=103. Based on this power calculation, the 120 participants recruited meant the study was adequately powered, even with data exclusions due to issues with TEWL measurement.

3.3.3 Procedure

In accordance for salivary sampling, participants were asked not to chew gum or drink caffeine, juice or alcohol 18 hours prior to the study and not to eat or brush their teeth in the hour before their session. Additionally, to prevent confounds with the TEWL measurements, they were asked not to apply moisturiser, shower or exercise in the hour before the session. Compliance with these instructions were checked at the beginning of the experimental session. All sessions were conducted between the hours of 12:30pm and 5:00pm to minimise the effects of diurnal rhythms on sCort and sAA (Strahler et al., 2017). Each 90-minute session took place at the University of Auckland Clinical Research Centre. Temperature and humidity of the experimental room was measured using an ambient condition sensor RHT 100 (Courage + Khazaka, Germany).

The experimental procedure is shown in Figure 1. After providing written informed consent, participants completed baseline measures including: questionnaires assessing demographics and psychological variables, a saliva sample and TEWL measures. Participants were then exposed to a standardised tape-stripping procedure to create skin barrier disruption. After this, participants completed the TEWL, psychological variables and saliva measurements again before being randomised to one of four interventions (control, comfort, music or Paro). Randomisation was performed by a researcher not involved in the experiment using a random number generator. Randomisation was concealed to the primary researcher until this point, where they opened a sealed envelope containing the group allocation.

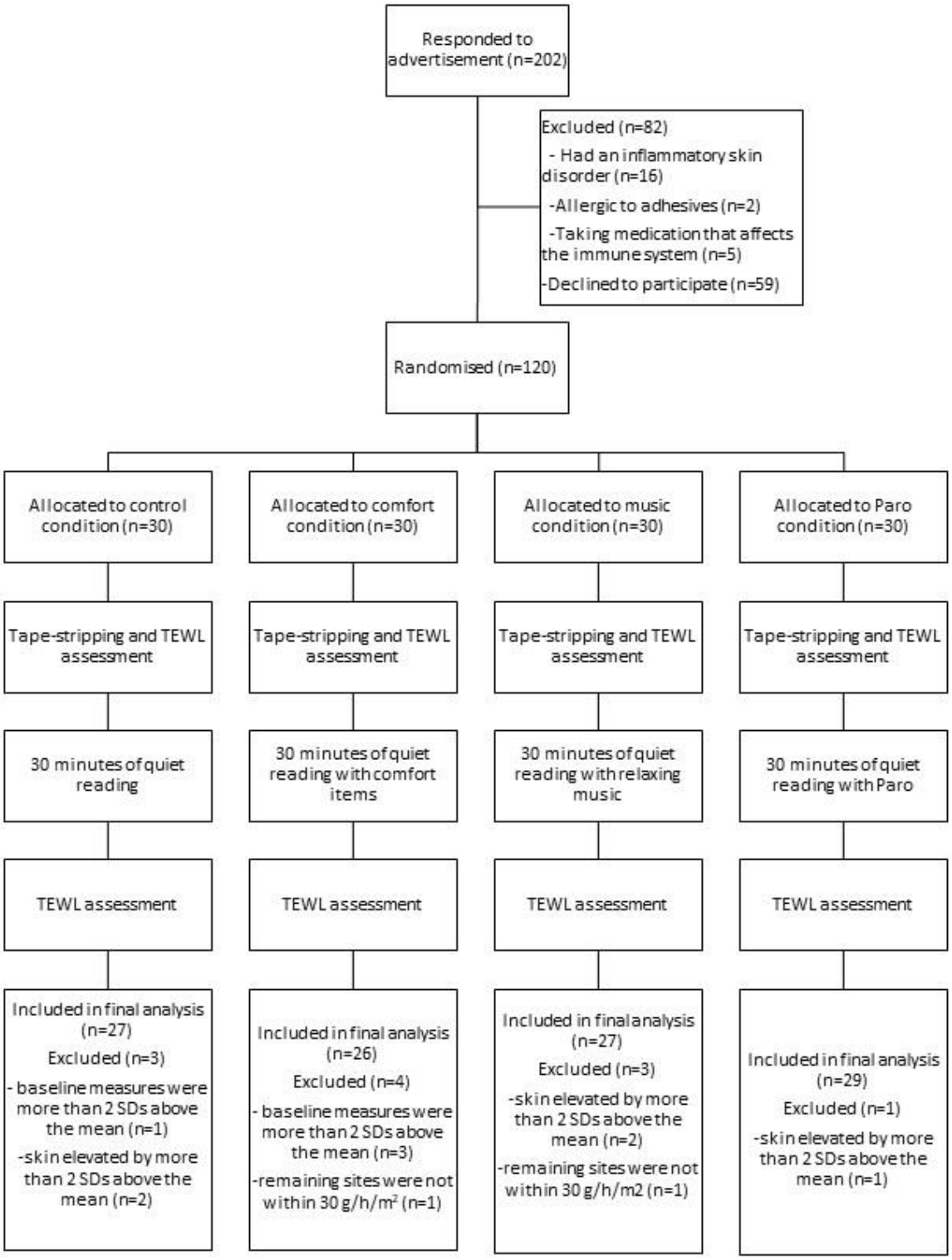


Figure 1. Overview of the study procedure and TEWL measurements.

Participants were introduced to their allocated intervention and asked to interact with their enrichment item during a 30-minute recovery period, while their experimental wound healed. A 30-minute period was chosen to investigate the immediate effect of the interventions on healing. Previous studies have successfully shown that psychological interventions can improve SBR from tape-stripping over this time-period (Robinson, Jarrett et al., 2015; Robinson, Ravikulan et al., 2017). Participants were asked to interact with their item as much as possible, not use any electronic devices, not touch their wound or pull down their sleeve, and not fall asleep. The researcher left the room and returned after 30 minutes. During this time, the participants were video-recorded so their compliance with instructions could be assessed. All measures were completed for a final time and participants were asked to rate how much they engaged with their item on a scale of 1 (not at all) to 5 (extremely). Upon completion of the study, participants were provided with a $40 voucher as compensation for their time.

3.3.4 Interventions

3.3.4.1 Comfort. The comfort condition was provided with tactile enrichment in the form of blankets and pillows. The participants in this condition were told to use these items throughout the 30-minute period to make themselves comfortable. This condition was seen as the human equivalent of the nestlets used in Vitalo and colleagues' (2009) study of healing in rodents. Like the nestlets, the blankets and pillows provided a sense of comfort and tactile enrichment.

3.3.4.2 Music. Participants in the music condition were provided with a selection of CDs, a personal CD player and headphones. The participants were asked to listen to music throughout the 30 minutes. They were free to choose tracks from the CD selection provided which all contained compilations of low-arousal relaxing or classical music. These genres

were chosen as they have been found to have the most reliable stress-reducing effects (Chafin et al., 2004).

3.3.4.3 Paro. Participants in the Paro condition were provided with the robot, Paro, and asked to interact with it for the 30-minute recovery period. They were instructed that they could talk to it, stroke it and cuddle it over the recovery period.

3.3.4.4 Control. The control condition was not provided with any form of EE other than magazines. All conditions were provided with magazines as this has been used as a control condition in previous research as a neutral activity to keep participants occupied during the 30-minute recovery period, so they did not become too bored (Robinson, Ravikulan et al., 2017; Skoluda et al., 2015).

3.3.5 Measures

As shown in Figure 1, all outcome measures were taken at three time-points throughout the session; at baseline, after tape-stripping and after the 30-minute recovery period.

3.3.5.1 Tape-stripping and SBR procedure. Tape-stripping is an experimental wound technique in which the top layer of skin, the stratum corneum, is removed by repeatedly applying and removing adhesive tape to create skin barrier disruption. Tape-stripping is a relevant model to observe wound healing in a non-invasive and inexpensive way which can also be assessed within a short time-frame. The procedure for the tape-stripping followed published methods used in previous research (Robinson, Jarrett et al., 2015).

Baseline skin barrier function was measured by obtaining readings of TEWL using a Tewameter TM300 probe (Courage + Khazaka, Germany), which measures the evaporation rate (in $g/m^2/h$) in the air layer adjacent to the skin (Koschwanez & Broadbent, 2011). TEWL indicates the ability of the skin to prevent water loss through the epidermis. A higher TEWL

value indicates a higher amount of water is evaporating through the epidermis and lower skin barrier function. TEWL increases when the skin is damaged and returns to baseline as the skin heals, providing an estimate of SBR (Koschwanez & Broadbent, 2011).

To measure TEWL, four $1cm^2$ areas were marked out on the inside of the participant's non-dominant forearm, 1cm below the elbow crease. The bottom site was a control site which remained undisrupted. Before the baseline measures, the Tewameter probe was heated to 34°C by a probe heater to ensure it was close to skin temperature. The participants placed their non-dominant forearm flat on a cushion and the probe was placed against each of the four marked sites, measuring each site for 60 seconds with one measurement being taken every second.

Once these baseline measures were obtained, the three test sites were dry shaved so that no hair was pulled out during the tape-stripping. The tape-stripping procedure used standard packaging tape (Scotch Commercial Grade Packaging Tape, 3M), which was applied to the three test sites with pressure and then carefully peeled off. This was repeated 20-40 times to remove the stratum corneum. After the first 20 strips, TEWL was measured to determine whether the skin barrier had been disrupted to a minimum of 15 $g/m^2/h$ above baseline. If the TEWL was not elevated enough, another 10 strips were applied and the skin barrier was tested again. Tape-stripping stopped when the skin barrier was elevated by at least 15 $g/m^2/h$ or after 40 strips. Once tape-stripping had ceased, all four sites were re-measured using the Tewameter to determine the level of skin barrier impairment caused by the tape-stripping procedure.

For the rest of the experiment, participants were asked to keep their forearm uncovered and not to touch or scratch their wound. At the end of the session, TEWL was again measured to investigate SBR. A faster return to baseline indicates faster healing.

3.3.5.2 TEWL analysis. 20 consecutive measurements with a standard deviation below 0.5 were averaged to give an overall TEWL value for each site and time-point. Using these values, SBR was calculated as a percentage based on the following formula;

$$(TEWL_{elevated} - TEWL_{recovery}) / (TEWL_{elevated} - TEWL_{baseline}) \times 100$$ (Robles, 2007)

A higher percentage indicates higher SBR overtime. There was large variation in TEWL across the sample. This could be due to many reasons, including the fact that the humidity and temperature of the experimental room was not controlled (Rogiers, 2001). The data was therefore screened to ensure only valid data was included. As shown in Figure 1, SBR values were excluded if; a reading was not taken at all three time-points (n=1), baseline TEWL reading was more than two SDs above the mean (n=4), and skin was damaged by more than two SDs of elevation above the mean (n=4), as these represented outliers in the data.

After this exclusion, if the SBR values of the remaining sites were all within 10 $g/m^2/h$ all sites were averaged. Otherwise, the closest two SBR values were averaged. If the remaining sites were not within 30 $g/m^2/h$ of each other, the values were excluded as this indicated that a reliable reading was not obtained (n=2). After exclusion there were 27 participants in the control condition, 27 in the music condition, 26 in the comfort condition and 29 in the Paro condition.

3.3.5.3 Salivary stress biomarkers. Saliva samples were collected at each of the three time-points as per protocol using SaliCaps collection device (IBL, Hamburg, Germany). These samples were taken to examine whether any of the interventions caused changes in stress biomarkers (sCort and sAA). Before the first sample was taken, participants rested for 15 minutes, while completing their baseline questionnaire. Participants were asked to rinse their mouths with water, before collecting saliva using the passive drooling technique. Participants were asked to collect their naturally secreted saliva in their mouths for two minutes by not

swallowing, before transferring the accumulated saliva to the SaliCap. The samples were stored at -20°C at the University of Auckland before they were shipped on dry ice to the University of Vienna, where they were stored at -20°C until analysis. sCort was measured using a commercially available enzyme-linked immunosorbent assay (ELISA, IBL, Hamburg, Germany). sAA was determined using a kinetic colorimetric test (for details, see Strahler et al., 2016) using reagents obtained by Roche (Roche Diagnostics, Mannheim, Germany). Intra- and inter-assay coefficients of variance of both tests were below 10%.

3.3.5.4 Demographics and psychological measures. At baseline participants were asked about their gender, age, weight, height, alcohol consumption, smoking status, medication, diet and sleep patterns. These behaviours were assessed as they can affect immune parameters and healing.

Alcohol consumption was assessed as how often the participant had reported drinking alcohol over the past three months from 0 (never) to 5 (everyday), as well as how many drinks they had on average on the days they did drink. Participants were also asked how often they engaged in 30 minutes or more of physical activity during an average week from 0 (never) to 7 (everyday). They were also asked to rate their diet over the past week from 1 (very poor) to 5 (very good). Lastly, participants were asked, over the past month, how many hours of sleep they usually had per night to assess sleep duration.

3.3.5.5 Perceived stress. The 10 item Perceived Stress Scale (PSS) (Cohen et al., 1994) was measured at baseline to evaluate the extent to which participants viewed their life as being stressful. Participants were asked how much they had felt a certain way over the last month on a scale of 0 (never) to 4 (very often). Scores were totalled to give a perceived stress score ranging from 0 to 40.

3.3.5.6 Psychological variables. Visual analogue scales were completed at each time-point to assess participants' current levels of stress, pain, anxiety, relaxation and stimulation. Participants were asked to mark a cross on a 100mm line to represent how they were currently feeling. The anchors on the visual analogue scales included: not at all stressed to extremely stressed; no sensation of pain to most sensation of pain imaginable; not at all anxious to very anxious; not at all relaxed to very relaxed; and very bored to very stimulated.

3.3.6 Statistical Analysis

Data was analysed using IBM SPSS Statistics 22. A 2-step hierarchical regression was conducted to analyse the effects of condition on SBR, controlling for known covariates in the first step of the model. A series of two-step hierarchical regressions were also conducted to analyse the effects of condition on the post-recovery levels of the salivary stress hormones and psychological variables, controlling for baseline levels of the outcomes in the first step of the models. Due to the categorical nature of the conditions, condition was dummy coded before being added to the analysis so that the three EE conditions (comfort, music and Paro) were compared to the control condition. The sCort and sAA data violated the assumption of normality and therefore was transformed using a natural log transformation and logged values were used.

3.4 Results

3.4.1 Sample characteristics

The baseline and demographic characteristics for the sample are shown in Table 1. A summary of the statistics of the secondary outcomes across the time-points and conditions is provided in Table 2.

Table 1

Summary of Demographic and Baseline Characteristics of Participants across Condition

Baseline variable	Control	Comfort	Music	Paro
Age (years) M(SD)	22.47(4.07)	24.00(6.45)	27.30(12.04)	24.80(6.73)
Gender, n(%)				
Female	20(67%)	18(60%)	21(70%)	18(60%)
Male	10(33%)	12(40%)	9(30%)	12(40%)
Ethnicity, n(%)				
NZ European	7(23%)	8(27%)	9(30%)	6(20%)
Chinese	7(23%)	10(33%)	5(17%)	8(27%)
Other	16(53%)	12(40%)	16(53%)	16(53%)
BMI M(SD)	23.11(3.93)	23.24(3.68)	22.18(5.00)	22.99(3.08)
Exercise (days/week), M(SD)	3.57(2.06)	3.90(2.19)	3.67(1.90)	4.17(1.80)
Sleep Duration (hours/night), M(SD)	7.27(0.91)	6.87(0.90)	7.10(0.89)	7.13(1.00)
PSS, M(SE)	13.60(1.49)	14.20(1.24)	15.93(1.06)	14.57(1.24)
Baseline TEWL, averaged across the disrupted sites ($g/m^2/h$), M(SD)	16.45(3.80)	17.34(7.24)	16.72(3.33)	16.36(3.44)
Room temperature (°C), M(SD)	25.71(1.00)	25.91(1.35)	25.78(1.14)	25.72(1.10)
Room humidity (%), M(SD)	46.52(6.68)	46.84(6.87)	46.31(6.08)	46.01(6.42)
Average level of skin barrier impairment across the disrupted sites($g/m^2/h$), M(SD)	18.92(8.28)	21.41(7.87)	17.31(8.13	19.06(9.33)
Number of strips used, n(%)				
20	10(33%)	8(27%)	11(37%)	10(33%)
30	9(30%)	15(50%)	11(37%)	9(30%)
40	11(37%)	7(23%)	8(27%)	11(37%)

Note: M=Mean, SD= Standard deviation, TEWL= Trans-epidermal water loss, %= Percentage of participants in that category.

Table 2

Summary Statistics of the Secondary Outcomes across Conditions at each Time-point

Variable	Condition	Baseline, M(SD)	Post tape-stripping, M(SD)	Post recovery period, M(SD)
VAS stress score	Control	40.67(27.32)	30.17(25.41)	16.70(19.66)
	Comfort	39.47(29.84)	26.73(25.88)	17.87(20.58)
	Music	40.83(26.00)	25.53(21.39)	13.47(13.86)
	Paro	41.33(26.96)	29.43(27.81)	19.93(23.04)
	Total	40.58(27.23)	27.97(24.98)	16.99(19.47)
VAS pain score	Control	5.33(11.06)	8.47(11.48)	2.20(3.43)
	Comfort	8.07(14.99)	14.80(14.90	6.57(10.26)
	Music	9.60(13.51)	12.17(12.75)	8.23(13.12)
	Paro	2.70(7.45)	8.73(6.60)	3.50(5.43)
	Total	6.43(12.23)	11.04(11.97)	5.13(9.14)
VAS anxiety score	Control	20.90(25.92)	16.83(22.72)	8.80(12.78)
	Comfort	19.40(21.17)	15.97(18.87)	12.23(16.19)
	Music	15.63(19.91)	13.37(17.19)	8.97(13.67)
	Paro	18.60(25.26)	11.73(16.78)	8.33(14.74)
	Total	18.63(22.99)	14.48(18.91)	9.58(14.30)
VAS relaxation score	Control	68.10(29.04)	76.03(23.58)	84.80(13.73)
	Comfort	68.53(23.06)	72.93(19.54)	76.77(21.10)
	Music	73.60(18.61)	77.47(15.00)	82.33(13.89)
	Paro	79.60(15.34)	75.27(25.22)	80.83(16.81)
	Total	72.46(22.33)	75.43(21.00)	81.18(16.701)
VAS stimulation score	Control	52.67(17.30)	42.47(22.75)	42.23(21.34)
	Comfort	53.83(16.91)	41.73(22.81)	47.30(20.99)
	Music	57.53(22.19)	49.30(23.29)	63.37(22.30)
	Paro	49.13(19.84)	43.87(23.31)	47.60(19.89)
	Total	53.29(19.17)	44.34(22.94)	50.13(22.35)
sCort (nmol/l)	Control	1.71(1.11)	1.80(1.72)	1.22(1.07)
	Comfort	2.22(1.57)	1.82(1.60)	1.12(0.72)
	Music	2.08(1.24)	2.03(2.11)	1.55(0.81)
	Paro	3.12(3.31)	2.12(1.67)	1.19(0.87)
	Total	2.28(2.06)	1.94(1.76)	1.27(0.88)
sAA (U/ml)	Control	33.39(28.10)	33.35(30.36)	38.82(36.22)

Comfort	44.36(40.22)	37.22(33.24)	38.82(36.22)
Music	43.03(35.46)	38.30(27.55)	44.39(43.03)
Paro	46.36(41.71)	44.19(40.41)	44.88(27.95)
Total	41.79(36.64)	38.27(33.05)	42.99(54.30)

Note: M= mean, SD= standard deviation, VAS= visual analogue scale.

3.4.2 SBR

Mean SBR across conditions is shown in Figure 2. A two-step hierarchical regression was conducted to analyse the effects of the dummy codes for condition on SBR. The coefficients and *F* change scores for Step 2 of the model are shown in Table 3. Step 1 of the regression model (containing the known covariates of age, room temperature, room humidity, number of strips used and level of skin barrier impairment) was significant, indicating that these covariates explained 47% of the variance in SBR. As shown in Table 3, adding the dummy codes for condition into Step 2 of the model did not significantly explain any additional variance in the model. As shown in Table 3, none of the dummy codes were significant predictors of SBR. This indicates that SBR was not significantly different between the EE conditions and the control condition.

Table 3

Regression Analysis Summaries for Step 2 in the Regression Models of Dummy Codes for Condition Predicting the Outcome Measures

Outcome	**Predictor**	***B***	***p***	**95% CI**	***ΔF***	***p***
SBR	(Constant)	58.48	0.078	[-6.67, 123.64]	0.20	0.895
	Comfort dummy code	1.24	0.733	[-5.94, 8.42]		
	Music dummy code	1.78	0.625	[-5.42, 8.97]		
	Paro dummy code	2.70	0.446	[-4.30, 9.70]		
Anxiety	(Constant)	0.33	0.879	[-4.02, 4.69]	0.85	0.468
	Comfort dummy code	4.04	0.156	[-1.56, 9.65]		
	Music dummy code	2.30	0.420	[-3.32, 7.92]		
	Paro dummy code	0.46	0.870	[-5.14, 6.07]		
Stress	(Constant)	-3.28	0.313	[-9.70, 3.14]	1.09	0.354
	Comfort dummy code	1.76	0.633	[-5.51, 9.02]		
	Music dummy code	-3.32	0.368	[-10.58, 3.95]		
	Paro dummy code	2.91	0.430	[-4.36, 10.17]		
Relaxation	(Constant)	66.84	<0.001*	[56.32, 77.37]	1.61	0.190
	Comfort dummy code	-8.15	0.046*	[-16.16, 0.13]		
	Music dummy code	-3.92	0.337	[-11.96, 4.13]		
	Paro dummy code	-7.00	0.092	[-15.15, 1.15]		
Pain	(Constant)	-0.97	0.334	[-2.94, 1.01]	2.54	0.060
	Comfort dummy code	2.74	0.049*	[0.01, 5.48]		
	Music dummy code	3.50	0.013*	[0.75, 6.25]		
	Paro dummy code	1.38	0.040*	[0.13, 5.60]		
Stimulation	(Constant)	17.15	0.005*	[5.25, 29.05]	5.22	0.002*
	Comfort dummy code	4.51	0.364	[-5.29, 14.31]		
	Music dummy code	18.82	<0.001*	[8.98, 28.65]		
	Paro dummy code	7.05	0.158	[-2.77, 16.87]		
lnsCort	(Constant)	-0.26	0.005*	[-0.44, -0.08]	4.70	0.004*
	Comfort dummy code	-0.10	0.409	[-0.35, 0.14]		
	Music dummy code	0.23	0.067	[-0.02, 0.49]		
	Paro dummy code	-0.22	0.086	[-0.44, 0.70]		
lnsAA	(Constant)	0.91	<0.001*	[0.44, 1.37]	1.45	0.232
	Comfort dummy code	-0.05	0.775	[-0.36, 0.27]		

Music dummy code	0.06	0.709	[-0.26, 0.38]
Paro dummy code	-0.25	0.119	[-0.57, 0.88]

Note: *p<0.05, 95% CI= 95% confidence interval's for *B*

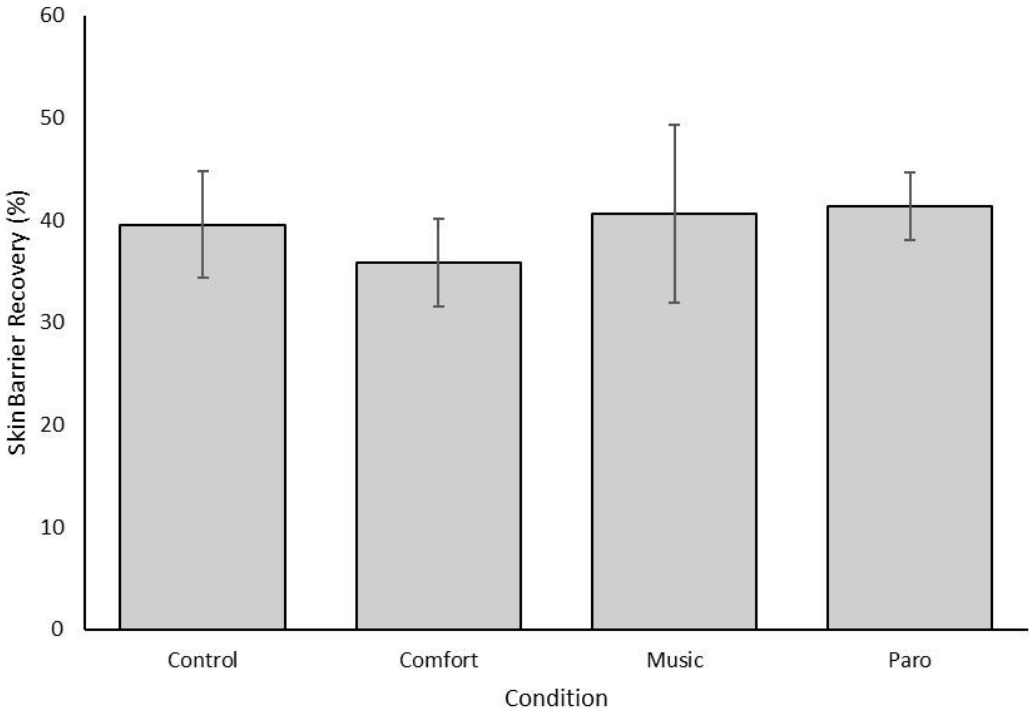


Figure 2. Mean SBR across conditions. Error bars represent 95% confidence intervals.

3.4.3 Psychological variables

A series of 2 step hierarchical regressions were conducted to analyse the effects of the dummy coded condition variables on the post-recovery levels of anxiety, stress, relaxation, pain and stimulation, controlling for the effects of baseline levels of the psychological variables in step 1 of the models. The coefficients and *F* change scores for step 2 of the models are shown in Table 3. Step 1 of the regression models for anxiety and stress was significant. However, as shown in Table 3, the *F* change score for step 2 and the dummy codes for condition were not significant. This indicates that the condition the participants

were assigned to did not affect the participants' levels of anxiety or stress after the recovery period.

As shown in Table 3, the *F* change score for step 2 of the regression model for post-recovery levels of relaxation was not significant. However, the dummy code for comfort vs. control was a significant predictor for relaxation levels at the post-recovery timepoint. The comfort condition had a lower relaxation score than the control condition by 8.16 points, when controlling for baseline relaxation. The other dummy codes for condition were not significant predictors in the model.

As shown in Table 3, the *F* change score for step 2 of the regression model for post-recovery levels of pain was not significant. However, all three dummy codes were significant predictors for pain post-recovery. Compared to the control condition, the comfort condition had a higher pain score by 2.74 points; the music condition had a higher pain score by 3.50 points, and the Paro condition had a higher pain score by 1.38 points, when controlling for baseline pain values.

As shown in Table 3, the *F* change score for step 2 of the regression model for the post-recovery levels of stimulation was significant, indicating that the regression model for stimulation was significantly improved by adding condition as a factor. The music vs. control dummy code was a significant predictor for stimulation levels post-recovery. The music condition had a 18.82 point higher stimulation score than the control condition at the post-recovery timepoint when controlling for baseline stimulation levels. The other dummy codes for condition were not significant predictors.

3.4.4 Salivary Stress Biomarkers

Two hierarchical regressions were conducted to analyse the effects of the dummy coded condition variables on naturally logged levels of sCort and sAA after the recovery period,

controlling for the effects of baseline salivary levels of the stress biomarker in the first step of the models. The coefficients and *F* change scores for these models are shown in Table 3. The *F* change score for the sCort model was significant, indicating that adding condition did improve the model. However, in both models, none of the individual dummy codes for condition were significant predictors. Therefore, adding condition did improve the model, but there was not enough evidence to conclude that any of the individual EE conditions improved cortisol at the post-recovery period compared to the control condition. The *F* change score for the sAA model was not significant, indicating that sAA levels were not affected by interaction with the EE compared to the control group.

3.5 Discussion

This study aimed to investigate whether three types of EE (comfort items, music or a Paro robot) could improve SBR after an experimental tape-stripping wound in a healthy population. Findings indicated no significant effects of these interventions on SBR compared to a control condition. However, analysis of the secondary outcomes demonstrated that the music condition had significantly higher stimulation levels and the comfort condition had significantly lower relaxation levels at the post-recovery timepoint compared to the control condition, when controlling for baseline levels. Lastly, the results indicated that all three EE conditions had significantly higher pain levels than the control condition. However, these pain scores were still relatively low, with no conditions having pain scores over 9/100 at the post-recovery time-point.

The finding that the music condition had higher stimulation levels after the recovery period compared to the control condition may be due to distraction. Previous studies suggest that music has beneficial effects because it can distract people from negative experiences

(Radstaak et al., 2014). Therefore, in this study, music may have alleviated the boredom of the 30-minute recovery period.

The finding that the comfort condition had lower relaxation levels than the control condition is unexpected, as it would be expected that the addition of blankets and pillows would increase relaxation. Some participants may have been unsure how best to use these items as instructed, which may have impacted their relaxation levels.

The null finding for SBR does not support Vitalo and colleagues (2009) study, which found that EE improved wound healing in stressed rats. One of the main theories for the beneficial effects of EE on healing is via stress reduction (Fricchione & Levine, 2017; Nachat-Kappes et al., 2012). Research also shows that psychological interventions, such as EE, are likely to only have an effect on immune parameters in stressed samples (G. E. Miller & Cohen, 2001). For example, Morley-Fletcher and colleagues (2003) found that EE only lowered the corticosterone levels of rats that were chronically stressed. In non-stressed rats, no effect of EE was observed.

Therefore, one reason for the null effects found in this study for SBR may be because the sample were not sufficiently stressed and therefore may benefit less from EE compared to a possible sample experiencing stress. The sample only had low to medium perceived stress levels at baseline, and the sCort levels were relatively low throughout the study. Future studies could investigate the effects of EE on stress reduction and wound healing in a more highly stressed sample or stress the sample experimentally. However, it may also be the case that these effects seen in animals, may not be readily transferred to human population.

Another reason for the limited effects found in this study could be because previous research on EE used non-active control groups (e.g. Paro compared to no Paro, or music compared to no music); however, the current study used an active control condition. All

conditions, including the control condition, had access to magazines during the recovery period. Magazines are a common control condition in research (Robinson, Ravikulan et al., 2017; Skoluda et al., 2015), as they provide a neutral activity; participants do not become too excited or enriched, but also do not become too bored which could lead to negative impacts from lack of stimulation such as an increase in negative affect. However, the magazines could have provided some cognitive enrichment and therefore had similar effects to the other conditions.

Research on EE has shown that sensory enrichment items that provide tactile comfort (such as the nestlets in Vitalo and colleagues' (2009) research and the equivalent blankets and Paro robot in the current study) or relaxation (as shown by research on the effects of music on stress (Chafin et al., 2004; Khalfa et al., 2003)) are key factors in how EE may improve wound healing through changes in immunological parameters and stress biomarkers. Cognitive enrichment can affect cognitive processes, such as memory and learning, but has little effect on immunological outcomes or wound healing. Therefore, the cognitive enrichment from the magazines may work through different mechanisms to sensory enrichment.

This study has several limitations. Firstly, the sample consisted of healthy participants, which makes it difficult to generalise the effects to clinical populations who are at risk of complications from poor wound healing (Guo & DiPietro, 2010). Future research could also investigate these effects in participants with inflammatory skin disorders, who have impaired skin barrier function and investigate further skin-specific outcomes. Furthermore, the experimental tape-stripping wound may not directly represent a real-life wound. Tape-stripping causes a minor skin wound which heals over a short time-frame. This makes it difficult to directly apply these findings to clinical wounds which have different healing

processes and heal over a longer period. However, a tape-stripping wound still offers some insight into how interventions may affect wound healing.

Lastly, the temperature and humidity of the experimental room varied between participants. Temperature and humidity can directly affect wound healing (Denda et al., 2007) and TEWL readings (Rogiers, 2001). Therefore, fluctuations in temperature and humidity may cause variation in the TEWL readings and possible inaccuracies in the measurements. Future research using tape-stripping should use a climate-controlled room where temperature and humidity are kept constant.

In conclusion, this study did not demonstrate that any of the EE interventions could improve SBR, or self-reported stress after an experimental tape-stripping wound compared to a control condition, although music did increase stimulation levels. Therefore, the effects of EE seen in animal research on wound healing may not be directly transferable to human populations. Despite these null results, the current study provides important knowledge on the potential effects of EE interventions in humans, informing future studies that will closely examine the mechanisms underlying EE interventions in stressed populations.

Chapter 4- The Effects of Sensory Enrichment After a Laboratory Stressor on Human Skin Barrier Recovery in a Randomised Trial

4.1 Preface

As discussed in the discussion section of Chapter 3, methodological limitations may have accounted for the lack of effects found in Study 1. Therefore, Study 2 was designed to amend the method to address these limitations and test the hypotheses again.

The first change was that Study 2 included the addition of a stress-inducing task after the tape-stripping procedure. This task was the Trier Social Stress Test (TSST), a standardised laboratory procedure that reliably induces increases in psychological and physiological stress (Kirschbaum et al., 1993). This stressor was included because it has been proposed that EE may only have an effect on immune parameters in stressed samples (G. E. Miller & Cohen, 2001; Morley-Fletcher et al., 2003). Therefore, in Study 1, there may have been a floor effect, whereby the participants were not sufficiently stressed to experience the stress-reducing effects of the EE interventions.

The control condition used was also changed for Study 2. Study 1 used an active control condition (reading magazines). However, this condition could also be a form of cognitive EE and therefore not an appropriate control condition to compare with the sensory EE interventions. Consequently, in Study 2 an inactive control condition was used, whereby participants were asked to sit quietly over the 30-minute intervention period. This change in the control condition removes the possible confounds from the magazines and allows for a truer comparison of the effects of providing EE interventions.

Lastly, Study 2 removed the comfort condition from the randomisation and therefore only used music and the Paro robot as EE interventions. Although the comfort condition was

included in Study 1 to be the human equivalent of the nestlets used in Vitalo and colleagues' (2009) study, this condition actually led to worse relaxation levels. Therefore, Study 2 aimed to investigate the effects of music and Paro, as forms of sensory EE, on SBR after a stressor. Study 2 also explored possible mediators of this relationship to help explain the mechanisms behind these effects.

4.1.1 Citation

Law, M., Jarrett, P., Nater, U. M., Skoluda, N., & Broadbent, E. (2020). The effects of sensory enrichment after a laboratory stressor on human skin barrier recovery in a randomized trial. *Psychosomatic Medicine*. https://doi.org/10.1097/PSY.0000000000000858

4.2 Introduction

EE is an intervention designed to facilitate sensory, cognitive, social, and physical stimulation by altering the environment through the provision of novel, controllable, and complex items (Khan et al., 2016). Generally, EE is used as an experimental approach in captive animals, but the term has also been applied to enriching human environments (Arranz et al., 2010). EE can be subdivided into multiple types; social (e.g. social support), sensory (e.g. visual, auditory or tactile stimulation), cognitive (e.g. puzzles) and motor (e.g. exercise) (Janssen et al., 2012; Singhal et al., 2014).

Research has shown that EE in rodents can improve cognitive functioning (Kotloski & Sutula, 2015), improve learning and memory (J. C. Bennett et al., 2006), protect against neurodegenerative disorders (Faherty et al., 2005), improve immune cell function (Arranz et al., 2010), and reduce the behavioural (Novaes et al., 2017) and physiological stress responses (Moncek et al., 2004). Although less researched, studies in humans have demonstrated that EE can decrease anxiety and depression (Daykin et al., 2008), improve cognitive functioning in older adults (De Oliveira et al., 2014), and improve activity levels (Janssen et al., 2014), depression, and cognitive functioning (Khan et al., 2016) in post-stroke patients.

One proposed mechanism behind these effects is that EE can buffer the stress response (Fairhurst et al., 2011; Nachat-Kappes et al., 2012). Most evidence indicates that EE is associated with the dampening of the stress response and an attenuation of the negative effects of stress (Dandi et al., 2018). Further to this, an inoculation stress hypothesis has been proposed, stating that positive, mild stress from living with EE can create resiliency against subsequent stressors (Crofton et al., 2015). For example, many studies have reported that enriched animals have lower corticosterone at baseline as well as in response to stress, indicating a reduction in HPA axis activity (Belz et al., 2003; Dandi et al., 2018). This results

in a buffering of the immunosuppressive effects of stress which leads to down-stream health benefits (Nachat-Kappes et al., 2012).

Despite this evidence, few studies have been conducted in human populations. Although humans already live in enriched environments, further enrichment can be added through the provision of sensory enhancement, social support, exercise, and education (Janssen et al., 2012; Sale, 2018; Singhal et al., 2014), but more rigorous research in humans is required. The current study aimed to investigate the effect of sensory enrichment on the healing of a tape-stripping wound in humans.

There is substantial evidence that stress can impair wound healing (Walburn et al., 2009) and that psychological interventions can improve the healing of both experimental and clinical wounds (Robinson, Norton et al., 2017). Interventions include; expressive writing (Koschwanez et al., 2013), relaxation (Robinson, Jarrett et al., 2015), social support (Robinson, Ravikulan et al., 2017), and mindfulness-based stress reduction (Meesters et al., 2018). EE has been proposed to reduce stress and therefore could be a further intervention to improve wound healing. One study found that rats provided with nesting material as tactile EE healed faster from burn wounds than non-enriched rats (Vitalo et al., 2009). However, this study is grounded in animal models and little research has been conducted in humans.

A recent study was the first to investigate the effects of sensory enrichment on wound healing in humans (Law, Jarrett et al., 2020a). Healthy participants underwent an experimental tape-stripping procedure to create a skin wound and were randomised to interact with one of three sensory enrichment interventions (tactile enrichment, music as auditory enrichment or a Paro robot as multi-sensory enrichment) or to an active control condition (reading magazines). There were no significant differences in wound healing or salivary stress-related biological measures between conditions, indicating that sensory enrichment

may not improve healing in humans. However, this study was limited by the use of an active control condition and low participant stress levels. The current study attempted to address these limitations by having an inactive control and by adding an experimental stressor.

As stated above, one of the main theories for the beneficial effects of EE is via stress-reduction (Fairhurst et al., 2011; Fricchione & Levine, 2017; Nachat-Kappes et al., 2012). To ensure that the study's sample was sufficiently stressed to experience the stress-reducing effects of sensory enrichment, the current study exposed participants to a laboratory stress task. The stress task was a version of the TSST (Kirschbaum et al., 1993), which is a well-validated procedure to invoke psychological stress.

The primary aim of this study was to investigate whether two different forms of sensory enrichment could improve wound healing in humans after laboratory stress. The forms of enrichment were [1] auditory enrichment through relaxing music, and [2] combination enrichment in the form of a Paro robot. Music was chosen as it can reduce stress levels (Khalfa et al., 2003) and improve immune parameters (Fancourt et al., 2014). The Paro robot is a companion robot designed to resemble a baby seal and provide comfort to users like a pet. Paro uses sensors to respond to the user's touch and voice through movements and noises, providing social, auditory, and motor enrichment. Paro also has soft fur which provides tactile enrichment. Research has shown that Paro can reduce subjective (McGlynn et al., 2016) and objective (Nomura & Hoshina, 2017; Robinson, MacDonald et al., 2015) stress, improve mood (Wada et al., 2005) and decrease loneliness (Robinson et al., 2013). Although the majority of research into the effects of Paro has been conducted in samples of older adults, research has also shown beneficial effects in younger adults. In studies with young healthy adults, interacting with Paro has been shown to decrease physiological stress responses as measured by skin conductance after a stressor (Aminuddin & Sharkey, 2017), increase brain activity (particularly in brain areas associated with positive emotional

processing) as measured by functional near-infrared spectroscopy (Kawaguchi et al., 2012), and increase social interaction (Wood et al., 2015). Therefore, we expected beneficial effects would occur in a healthy young adult sample.

The current study used the tape-stripping model to assess SBR. The upper layer of skin, the stratum corneum, is removed using adhesive tape so that the healing of the skin barrier can be examined (Gouin & Kiecolt-Glaser, 2011). This procedure has been used in previous research to demonstrate that stress can impair healing (Robles, 2007), and that psychological interventions, such as social support, can improve healing (Robinson, Ravikulan et al., 2017). The primary outcome of this study was SBR, as measured via changes in TEWL (described in detail below). Secondary outcomes included biological stress indices (sCort and sAA), psychological variables, BP and HR.

The primary hypothesis was that the two sensory enrichment conditions would show faster SBR compared to the control condition after the stressor. It was also hypothesised that the relationship between SBR and condition would be mediated by changes in the objective and subjective stress measures.

4.3 Method

4.3.1 Design

A 3(time-point) x 3(condition) mixed factorial randomised trial was performed to assess the effects of sensory enrichment (control v music v Paro) on SBR after a stressor and after tape-stripping.

4.3.2 Sample

A sample of 105 healthy adults (75 female, 30 male; average age 27.07 years; range=18-63 years) was recruited from the community using flyers and email advertisements.

Participants were included if they were over the age of 16 and spoke fluent English. Participants were excluded if they were allergic to tape or adhesives, had an inflammatory skin disorder (e.g. eczema), were taking medications that affected the immune system (e.g. corticosteroids) or were pregnant. Ethics Approval was granted by the University of Auckland Human Participants Ethics Committee.

4.3.2.1 Power analysis. The sample size was calculated using G*Power (Faul et al., 2007), and a 3(conditions) x 3(time-points) mixed ANOVA. A power level of .80 and alpha level of .05 were chosen and an expected effect size of F=0.28 was estimated from a previous study on changes in SBR due to relaxation (Robinson, Jarrett et al., 2015). These parameters led to a required sample size of 87. This sample size was increased by 20% due to possible errors in TEWL measurements, giving a total sample size of 105.

4.3.3 Procedure

Data collection took place between June 2018 and December 2018. In accordance with salivary sampling procedures, participants were asked not to drink caffeine, juice or alcohol in the 18 hours and eat in the hour before the session. They were also asked not to apply moisturiser, shower or exercise in the hour before to prevent confounds with the TEWL measurements. The experimental sessions lasted two hours and were conducted between the hours of 12:30pm and 5pm to minimise variability caused by the diurnal rhythms on the salivary stress-related biological measures (Fries et al., 2009). Temperature and humidity of the experimental room were measured using an ambient condition sensor RHT 100 (Courage + Khazaka, Germany). A dehumidifier was running to minimise possible confounds in TEWL measurements due to high ambient humidity.

The full procedure for the experimental session is provided in Figure 3. After providing informed consent, participants completed baseline measurements including a questionnaire

assessing demographics, health-related behaviours and psychological variables, a BP and HR recording and a saliva sample. Participants were then exposed to a standardised tape-stripping procedure to create skin barrier disruption.

After the tape-stripping procedure, participants were exposed to a shortened version of the TSST to elicit stress (Kirschbaum et al., 1993). Participants were given three minutes to prepare and five minutes to present a speech on their dream job. Participants were told their speech would be recorded and that a panel of judges would review it and award the best speech a $100 voucher. A shortened version of the TSST, with the inclusion of only the speech-task, has been found to be as effective as the full version in eliciting physiological stress responses (Goodman et al., 2017).

After the stress task, participants completed measures of psychological variables, BP, HR and saliva again before being randomised to one of three conditions (control, Paro or music). Randomisation was conducted by a researcher uninvolved in the project via a random number generator. Group allocation was concealed to the lead researcher until this point, where the researcher opened a sealed envelope which contained the participants' assigned condition.

Participants were then introduced to their allocated intervention and asked to interact with their item or sit quietly during a 30-minute intervention period, while their wound healed. This time-period was chosen as research has shown that the greatest healing of the skin barrier occurs in the first 30-minutes after tape-stripping (Robles, 2007). Participants were asked not to use any electronic devices, touch, scratch or cover their wound, or fall asleep. During this period, the participants were video-recorded to ensure compliance with instructions. The researcher left the room and returned once 30-minutes had elapsed. All measures were then completed for a final time. Participants were provided with a $40 voucher at completion of the study.

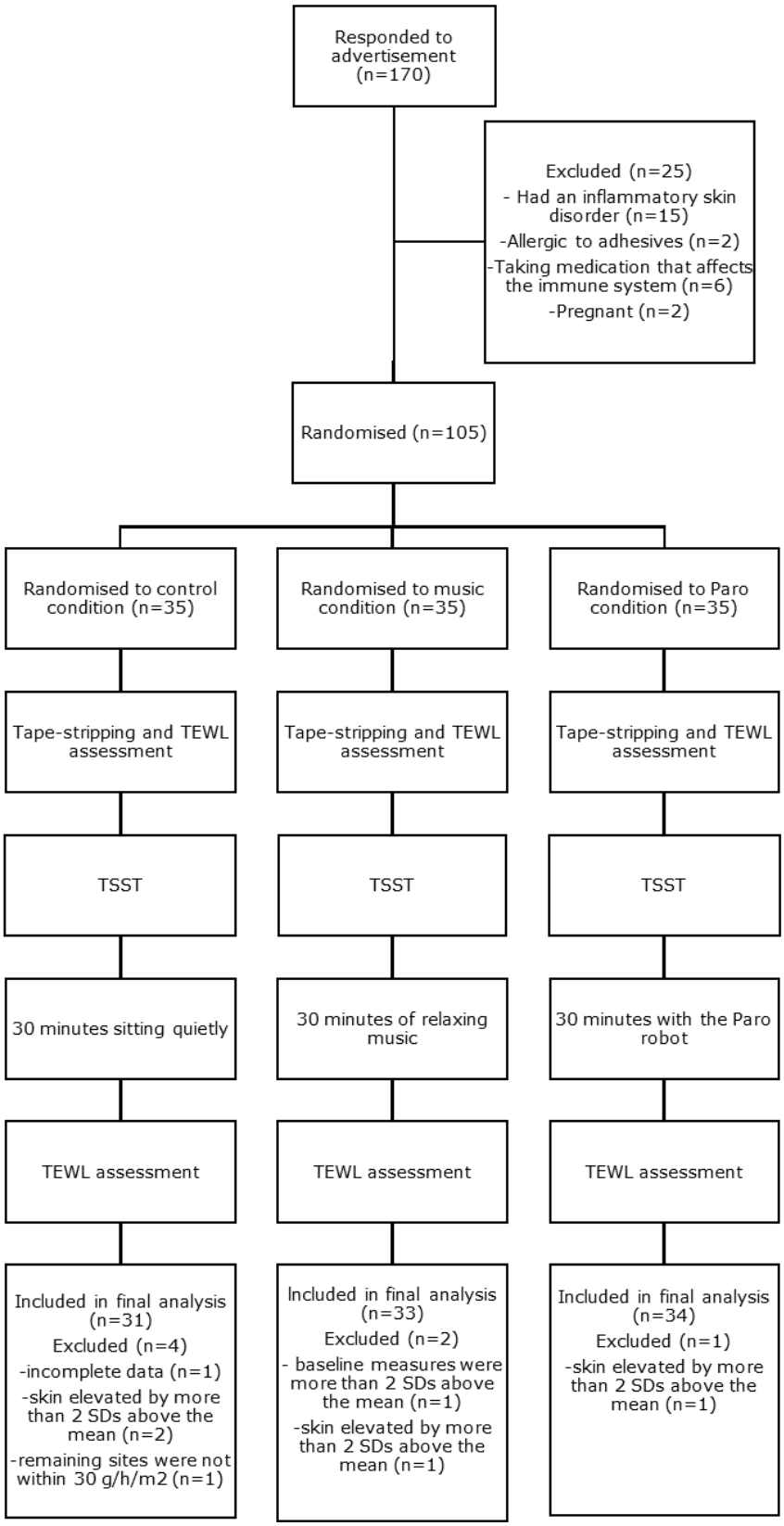


Figure 3. Overview of the study procedure and TEWL measurements.

4.3.4 Interventions

4.3.4.1 Paro. Participants in the Paro condition, were introduced to the robot Paro, as shown in Figure 4a, and asked to interact with it over the 30-minute intervention period. They were told that they could talk to it, stroke it and cuddle it over the intervention period.

(a) **(b)**

Figure 4. Photos of the two environmental enrichment interventions; (a) the Paro condition and (b) music condition.

4.3.4.2 Music. Participants in the music condition were provided with a set of CDs containing compilations of relaxing and low-arousal music, a CD player and headphones, as shown in Figure 4b. Participants were asked to listen to music throughout the 30-minute intervention period. They were free to choose whichever tracks they wanted to listen to in order to give participants an aspect of choice and control, an important part of EE (Leardi et al., 2007). Low-arousal music was chosen as these genres have been found to have the most reliable stress-reducing effects (Radstaak et al., 2014).

4.3.4.3 Control. The participants under the control condition were not given any form of enrichment and were asked to sit quietly for the 30-minute period.

4.3.5 Tape-Stripping Procedure

Tape-stripping is an experimental wound technique that uses the repeated application of adhesive tape to remove the upper layer of skin, the stratum corneum, to create skin barrier disruption. Tape stripping is a standardised model of wound healing that is non-invasive, inexpensive and can be measured in a short time-frame (Wilhelm et al., 2017). The procedure for the tape-stripping followed standardised methods (Law, Jarrett et al., 2020a; Robinson, Jarrett et al., 2015; Robles, 2007).

Baseline skin barrier function was measured using a Tewameter 300 probe (Courage + Khazaka, Germany). This probe measures the evaporation rate (in $g/m^2/h$) in the air layer adjacent to the skin (Meesters et al., 2018) giving an indication of TEWL; the ability of the skin to prevent water loss. A higher TEWL value indicates a higher amount of water is evaporating through the epidermis. TEWL increases when the stratum corneum is damaged and decreases as it heals (Koschwanez & Broadbent, 2011). Four $1cm^2$ sites were marked on the inside of the participants' non-dominant forearm, 1cm below the elbow crease, using a template. The bottom site was a control site which remained undisrupted. Before measurements were taken, the Tewameter was heated to 34°C to ensure it was skin temperature for a reliable reading. The participants placed their forearm flat on a cushion and the probe was placed against each of the four sites, measuring for 60 seconds, with one measurement being taken every second.

Once these measurements were acquired, the top three test sites were dry shaved to ensure no hair was pulled out during tape-stripping. Scotch Commercial Grade Packaging Tape, 3M, was applied to the three test sites with pressure and then carefully peeled off. This was

repeated 10-40 times to remove the stratum corneum. A new piece of tape was used after each application. After 10 strips, the TEWL of the top site was measured to assess whether the skin barrier had been disrupted to at least 15g/m^{2}h above baseline. If this elevation level was not reached, another 10 strips were applied, and the site was re-measured. The tape-stripping procedure ceased once the skin barrier was elevated by at least 15g/m^2/h or after 40 strips. After the tape-stripping procedure was stopped, the TEWL of each site was again measured to determine the level of skin barrier impairment caused by the tape-stripping. After the intervention period, TEWL was measured to determine how well the wound had healed, as indexed by SBR.

4.3.5.1 SBR analysis. 20 consecutive measurements with a standard deviation below 0.5 were averaged to give an overall TEWL value for each site and time-point. Using these values, SBR was calculated for each site as a percentage using the following formula;

$(TEWL_{elevated} - TEWL_{recovery}) / (TEWL_{elevated} - TEWL_{baseline}) \times 100$ (Robles, 2007)

A higher percentage indicates higher SBR over the experimental session. Similar to previous research (Law, Jarrett et al., 2020a; Robinson, Jarrett et al., 2015; Robinson, Ravikulan et al., 2017) the data was screened for outliers to ensure only valid data was included. As shown in Figure 3, SBR values were excluded if: there was incomplete data (*n*=1), the baseline reading was more than two standard deviations above the mean (*n*=1), and skin was damaged by more than two standard deviations above the mean elevation of the sample (*n*=4).

After this initial exclusion, if the SBR values of the remaining sites were within 10g/m^2/h of each other, the sites were averaged. Otherwise, the closest two values were averaged. If the remaining sites were not within 30g/m^2/h of each other, the values were excluded as this indicates a reliable reading was not obtained (*n*=1). After these exclusions, there were 31

participants (23 females and 8 males) in the control condition, 33 (26 females and 7 males) in the music condition and 34 (22 females and 12 males) in the Paro condition.

4.3.6 Measures

4.3.6.1 Salivary stress-related biological measures. Saliva samples were collected at baseline, after the stressor and after the intervention period, as per protocol using SaliCaps collection device (IBL, Hamburg, Germany). These samples were taken to examine changes in the concentrations of the salivary stress-related biological measures, sCort and sAA, due to the experimental tasks. Participants rinsed their mouths with water, before collecting saliva using the passive drool technique. Participants were asked not to swallow for two minutes in order to collect their naturally secreted saliva in their mouths, which was then transferred into the SaliCap through a straw. The samples were stored at -20°C at the University of Auckland, before being shipped on dry ice to the University of Vienna for analysis. Concentrations of sCort were measured using commercially available enzyme-linked immunosorbent assay (ELISA, IBL, Hamburg, Germany). sAA activity was determined using a kinetic colorimetric test (Strahler et al., 2016) using reagents obtained by Roche (Roche Diagnostics, Mannheim, Germany). Intra- and inter-assay coefficients of variance of both tests were below 10%.

4.3.6.2 Cardiovascular measures. Participants' BP and HR rate were measured at baseline, after the stressor and after the intervention period using a fully automated BP monitor (Healthtec, New Zealand).

4.3.6.3 Psychological variables. Self-reported stress, relaxation and stimulation were measured at baseline, post-stressor and post-intervention period using 100mm visual analogue scales. Participants were asked to mark a cross on a 100mm line to represent how

they were currently feeling. The anchors on the scales were; not at all stressed to extremely stressed; not at all relaxed to very relaxed; and very bored to very stimulated.

4.3.6.4 Demographics and health behaviours. At baseline, participants were asked their sex, age, height, weight and ethnicity. Alcohol consumption was measured as how often the participant reported drinking alcohol over the past three months from 0 (never) to 5 (everyday), as well as how many drinks they had on average on the days they did drink. Participants were asked how often they engaged in at least 30 minutes of physical activity on average from 0 (never) to 7 (everyday). Participants were also asked to rate the quality of their diet over the past week from 1 (very poor) to 5 (very good). Lastly, they were asked how many hours of actual sleep they usually had per night.

4.3.6.5 Perceived stress. The 10 item PSS (Cohen et al., 1994) was administered at baseline to assess the extent to which participants viewed their life as stressful. Participants were asked how much they felt a certain way over the last month on a scale of 0 (never) to 4 (very often).

4.3.6.6 Enjoyment of the intervention period. After the intervention period, participants were asked to rate on a scale of 0 (not at all) to 4 (extremely) how much they enjoyed the intervention period.

4.3.6.7 Observational coding of the intervention period. The degree of engagement with the enrichment items was observationally coded from the video-recordings of the 30-minute intervention period. The lead author coded each participant's interaction with their enrichment item on a scale from 0 to 4. The Paro condition was rated from 0 (no interaction), 1 (interaction for less than 1/3 of the intervention period), 2 (interaction for 1/3 to 2/3 of the intervention period), 3 (interaction for most of the intervention period), 4 (interaction for the

entire intervention period). The music condition was rated from 0 (did not play the music), 1 (music was playing for less than 1/2 of the time), 2 (music was playing for most, but not the entire intervention period), 3 (music was playing the entire intervention period), 4 (music was playing the entire intervention period with physical engagement e.g. movement or singing/humming).

4.3.7 Statistical Analysis

Data was analysed using IBM SPSS Statistics 22. An ANOVA was conducted to assess the differences in SBR between conditions, as well as an ANCOVA (controlling for covariates). Mixed factorial ANOVAs were conducted to analyse the interaction and main effects of time-point and condition on the psychological variables, cardiovascular variables and salivary stress-related biological measures. The sCort and sAA data violated the assumption of normality for ANOVAs and were therefore transformed using a natural log transformation and logged values (lnsCort and lnsAA) were used in the analysis.

Exploratory mediational analysis was conducted with bootstrapping, using the PROCESS macro for SPSS, version 3 (Hayes, 2017) to investigate whether enjoyment mediated the relationship between condition and SBR. All tests were reported using the Greenhouse-Geisser adjustment due to violations in sphericity. All significant interaction effects were followed up using simple pairwise comparisons with Bonferroni corrections.

4.4 Results

4.4.1 Baseline Characteristics

The baseline and demographic characteristics for the sample are shown in Table 4; no differences were found between conditions.

Table 4

Summary of Demographic and Baseline Characteristics across Conditions

Baseline variable	Control	Music	Paro	p-value
Age (years), M(SD), range	26.91(11.17), 18-63	26.57(8.04), 18-51	27.71(10.43), 18-62	.89[a]
Sex, n(%)				.38[b]
Female	24(69%)	28(80%)	23(66%)	
Male	11(31%)	7(20%)	12(34%)	
Ethnicity, n(%)				.90[b]
NZ European	9(26%)	8(23%)	10(29%)	
Indian	4(11%)	7(20%)	6(17%)	
Other Asian	8(23%)	10(29%)	9(26%)	
Other	14(40%)	10(29%)	10(29%)	
BMI, M(SD)	23.28(4.30)	24.26(5.03)	24.67(3.41)	.39[a]
Exercise (days/week), M(SD)	3.77(1.40)	4.23(1.93)	3.29(1.71)	.07[a]
Diet Quality, M(SD)	3.49(0.82)	3.40(0.77)	3.31(0.87)	.68[a]
Sleep (hours/night), M(SD)	7.27(0.92)	7.00(1.00)	7.13(0.93)	.49[a]
PSS, M(SD)	16.68(6.32)	17.59(6.21)	17.43(6.60)	.84[a]
Systolic BP (mmHg), M(SD)	115.69(14.58)	114.07(13.88)	118.26(12.17)	.44[a]
Diastolic BP (mmHg), M(SD)	63.94(9.16)	66.12(10.61)	67.99(10.02)	.24[a]
HR (bpm), M(SD)	73.70(11.86)	74.15(8.74)	72.59(10.82)	.82[a]
sCort (nmol/l) M(SD)	2.75(1.71)	1.98(1.19)	2.60(2.48)	.19[a]
sAA (U/ml), M(SD)	54.51(53.33)	49.42(52.54)	64.11(53.52)	.50[a]
Baseline TEWL, averaged across sites (g/m^2/h), M(SD)	17.70(2.70)	17.43(2.62)	17.41(2.49)	.87[a]
Level of skin barrier impairment across disrupted sites(g/m^2/h), M(SD)	22.53(12.28)	22.41(10.18)	21.52(13.28)	.93[a]
Number of strips used, n(%)				.29[b]
10	14(40%)	8(23%)	6(17%)	
20	17(49%)	19(54%)	21(60%)	

30	2(6%)	6(17%)	7(20%)	
40	2(6%)	2(6%)	1(3%)	
Room temperature (°C),	25.03(1.34),	25.36(3.27),	24.79(1.51),	.56[a]
M(SD), range	22.00-27.50	22.23-27.30	20.40-27.10	
Room humidity (%), M(SD),	43.26(5.50),	43.25(6.74),	44.90(5.60),	.42[a]
range	32.70-54.30	34.87-55.70	33.90-59.00	

Note: M=Mean, SD= Standard deviation, %= percentage of participants in that category. P-value was calculated by one-way ANOVAs[a] and Chi-square tests[b]

4.4.2 Observed Engagement with Enrichment Items

On average, participants in the Paro condition engaged with Paro most of or all of the intervention period (*M*=3.43, *SD*=0.85). All participants in the music condition played the music for the entire intervention period, with many of the participants also physically engaging with the music through movement or singing/humming (*M*=3.43, *SD*=0.56). Engagement levels were not significantly associated with any of the outcomes and so were not controlled for in any subsequent analyses.

4.4.3 SBR

A one-way ANOVA showed that SBR significantly differed between conditions ($F_{(2,97)}$=3.81, *p*=.026, η_p^2=.07). Follow-up tests using bonferroni comparisons demonstrated that the Paro condition had significantly higher SBR (*M*=45.10, *SD*=12.78) than the control condition (*M*=36.37, *SD*=13.33, *p*=.022, *d*=0.67). The music condition (*M*=41.71, *SD*=12.32) did not significantly differ from either the Paro (*p*=.845, *d*=0.27) or control conditions (*p*=.295, *d*=0.42).

Body max index (BMI) (*r*=.224, *p*=.027) and level of skin barrier impairment (*r*=-.473, *p*>.001) were significantly correlated with SBR. An ANCOVA was conducted to analyse differences in SBR between conditions when controlling for these covariates as well as other

covariates known to be associated with SBR including: humidity, temperature, age and number of strips (Fluhr & Darlenski, 2014). When controlling for these covariates, a significant difference in SBR was found between conditions ($F_{(2,88)}$=3.25, p=.043, η_p^2=.07). As shown in Figure 5, the adjusted means showed that the Paro condition had significantly higher SBR compared to the control condition (p=.040). The music condition did not differ from the other conditions (ps<.05).

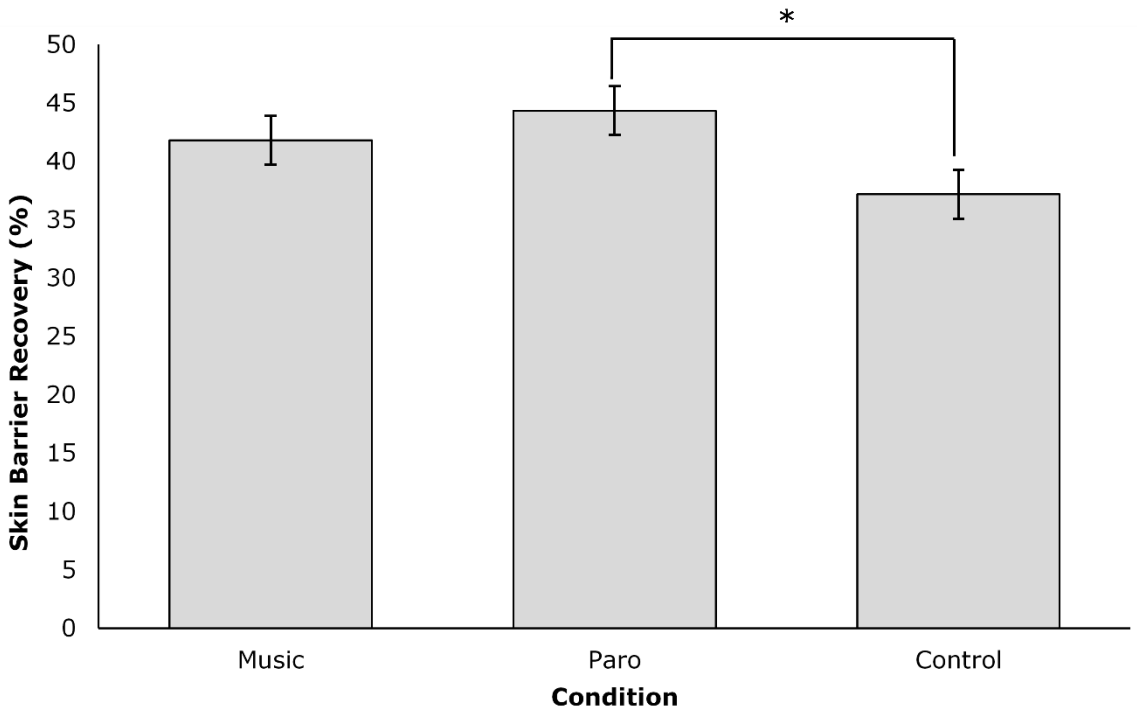


Figure 5. Adjusted mean SBR with standard error bars for each condition, controlling for covariates. *Note*: *p<.05.

4.4.4 Psychological Variables

Mixed ANOVAs showed a significant main effect of condition for stress ($F_{(2,102)}$=3.30, p=.041, η_p^2=.06), however, follow-up pairwise comparisons did not show any significant differences across conditions. There were no main effects of condition for relaxation or stimulation.

There were main effects of time-point for all psychological variables; stress ($F_{(2,194)}$=86.74, p<.001, η_p^2=.46), relaxation ($F_{(2,189)}$=49.42, p<.001, η_p^2=.33) and stimulation ($F_{(2,178)}$=60.44, p<.001, η_p^2=.38). The post-hoc tests are provided in Table 5. Irrespective of condition, the stressor led to an increase in stress and stimulation and a decrease in relaxation. In contrast, the intervention period led to a decrease in stress and stimulation to below baseline levels and an increase in relaxation.

Table 5

Summary Statistics and Post-hoc Comparisons for the Secondary Outcomes across Time

Task		Baseline	Post-stressor	Post-intervention
Psychological Variables	Stress, M(SD)	40.48(26.13) b*c**	47.85(26.31) a*c**	17.84(16.69) a**b**
	Relaxation, M(SD)	64.98(24.03) b**c**	52.75(26.25) a**c**	78.18(24.03) a**b**
	Stimulation, M(SD)	53.57(18.77) b**c**	68.33(18.15) a**c**	40.85(24.38) a**b**
Cardiovascular Variables	Systolic BP (mmHg), M(SD)	116.01(13.56) b**c**	120.96(14.23) a**c*	110.85(18.98) a**b*
	Diastolic BP (mmHg), M(SD)	66.02(10.01) b**	69.00(10.56) a**c**	64.67(10.18) b**
	HR (bpm), M(SD)	73.47(10.49) c**	72.11(10.76) c**	69.13(8.39) a**b**
Stress-Related Biological Measures	lnsCort, M(SD)	0.65(0.69) c**	0.62(0.65) c**	0.38(0.60) a**b**
	lnsAA, M(SD)	3.55(1.02) c*	3.62(1.01) c**	3.32(0.96) a*b**

Note: a=different to baseline, b= different to post-stressor, c= different to post-intervention, *p<.05, **p<.001

A significant interaction effect was observed for time-point and condition on stimulation ($F_{(4,178)}$=3.60, p=.010, η_p^2=.07). Follow-up one-way ANOVAs revealed a significant difference in stimulation between conditions post-intervention ($F_{(2,103)}$=3.37, p=.038). The music condition rated themselves as being significantly more stimulated (M=48.63, SD=24.19) than the control condition after the intervention period (M=34.03, SD=21.43, p=.034). The Paro condition (M=40.00, SD=25.26) did not significantly differ from either the control (p=.89) or music conditions (p=.40). No significant interaction effects were observed for stress or relaxation (all ps>.05).

4.4.5 Cardiovascular Variables

Mixed ANOVAs showed significant main effects of time-point for systolic BP ($F_{(2,158)}$=20.86, p<.001, η_p^2=.71), diastolic BP ($F_{(2, 192)}$=16.26, p<.001, η_p^2=.14) and HR ($F_{(2,200)}$=24.08, p<.001, η_p^2=.19). The post-hoc tests are provided in Table 5. Irrespective of condition, the stressor led to an increase in systolic BP and diastolic BP and the intervention period led to a decrease in systolic BP, diastolic BP and HR. There were no main effects of condition or interaction effects for any of the cardiovascular variables (ps>.05).

4.4.6 Salivary Stress-Related Biological Measures

Mixed ANOVAS found no significant main effects of condition for sCort or sAA. There was a main effect of time-point for both sCort ($F_{(2,167)}$=18.87, p<.001, η_p^2=.16) and sAA ($F_{(2,188)}$=7.76, p=.001, η_p^2=.07). The post-hoc tests are shown in Table 5. This indicates that salivary stress-related biological measure levels were the lowest after the intervention in all conditions.

There were no significant interaction effects between condition and time-point for either sCort ($F_{(3,167)}$=1.24, p=.297, η_p^2=.02) or sAA ($F_{(4,188)}$=0.22, p=.918, η_p^2=.00).

4.4.7 Mediational Analyses

It was hypothesised that stress would mediate the relationship between SBR and condition. Greater SBR was associated with a decrease in self-reported stress from post-stressor to post-intervention in the total sample (r=-.21, p=.042). However, change in self-reported stress was not significantly different between conditions. Further exploratory analysis was conducted to investigate other possible mediators of this relationship. Self-reported enjoyment (r=.32, p=.001) during the intervention period was significantly correlated with SBR. No other outcomes (including observed engagement, relaxation and stimulation levels, cardiovascular or biological stress-related markers) were significantly correlated with SBR, so could not be included as possible mediators. A one-way ANOVA showed a significant difference in enjoyment between conditions ($F_{(2,102)}$=17.44, p<.001), with the control condition having significantly lower enjoyment levels (M=2.34, SD=0.94) than both the Paro (M=3.11, SD=0.93, p=.002) and music conditions (M=3.66, SD=0.94, p<.001), which did not significantly differ from each other.

A series of regressions were used to test whether the relationship between condition and SBR was mediated by enjoyment during the intervention period (Hayes, 2017). The mediational model is presented in Figure 6. As the predictor was multi-categorical, condition was dummy-coded so that pathway 1 represented the music vs control conditions and pathway 2 represented the Paro vs control conditions.

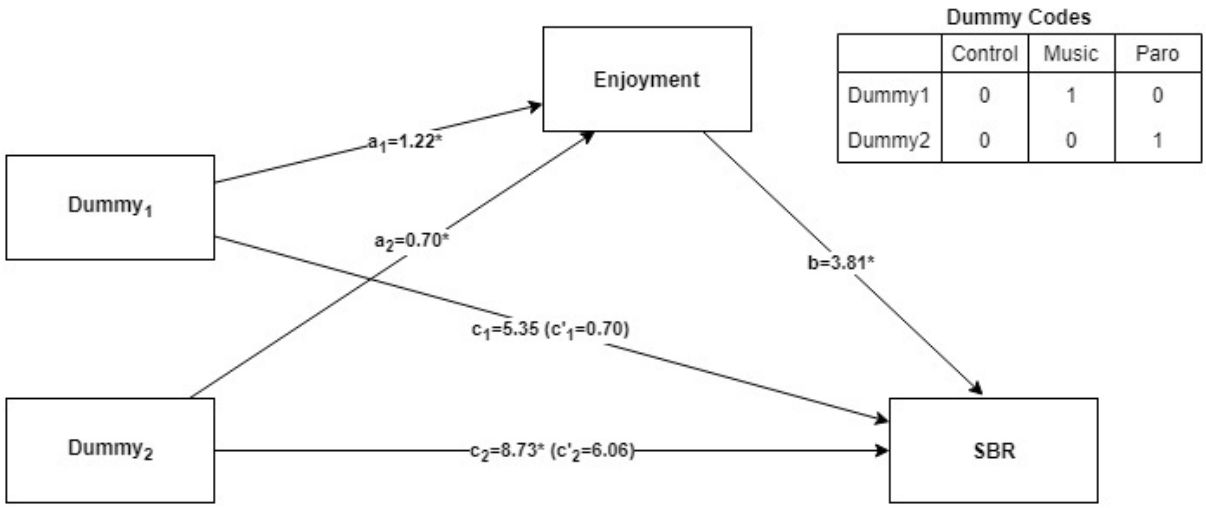


Figure 6. Mediation model with unstandardized regression coefficients for the relationship between the dummy coded conditions and SBR, with enjoyment as the mediator. *Note: *p*<.05.

In step 1 of the mediation model, the regression for the effect of the Paro dummy variable on SBR, ignoring the mediator (pathway c_2), was significant (*b*= 8.73, $t_{(95)}$=2.75, *p*=.007) indicating the Paro condition had higher SBR compared to the control condition. The regression for the effect of the music dummy variable on SBR, ignoring the mediator (pathway c_1) was not significant (*b*= 5.35, $t_{(95)}$=1.67, *p*=.098) indicating no significant difference in SBR between the music and control conditions. In step 2 of the mediation model, both regressions for the effect of condition on enjoyment were significant; music (pathway a_1) (*b*= 1.22, $t_{(95)}$=5.184, *p*<.001) and Paro (pathway a_2) (*b*= 0.70, $t_{(95)}$=3.00, *p*=.003). This demonstrates that both the Paro and music conditions had higher enjoyment levels during the intervention period than the control condition. In step 3 of the model, the regression for the effect of enjoyment on SBR in all conditions (pathway b) was significant (*b*= 3.81, $t_{(94)}$=2.82, *p*=.006), indicating that higher enjoyment levels were associated with increased SBR.

In the final step of the model, both regressions for the effect of condition on SBR, controlling for enjoyment, were not significant; music (pathway c'_1) (*b*= 0.70, $t_{(94)}$=0.20,

p=.84) and Paro (pathway c'$_2$) (*b*= 6.06, $t_{(94)}$=1.89, *p*=.062). This indicates that when controlling for enjoyment, the relationship between condition and SBR was reduced. The bootstrapped confidence intervals derived from 5000 samples indicated that the indirect effect coefficient was significant for both dummy variables, and Sobel's tests confirmed this significance; music (X1 indirect=4.64, *SE*=1.63, 95% CI[1.64,8.04], *z*=2.44, *p*=.015) and Paro (X2 indirect=2.67, *SE*=1.23, 95% CI[0.59,5.31], *z*=2.00, *p*=.046). Therefore, this model demonstrates significant mediation for enjoyment on the relationship between condition and SBR.

4.5 Discussion

This study aimed to investigate whether sensory enrichment in the form of music or a Paro robot after a laboratory stressor could improve SBR after a tape-stripping wound. Findings indicated that the Paro condition had significantly higher SBR after the intervention period compared to the control condition. However, no significant improvement in healing was found for the music condition, even though both conditions were hypothesised to improve healing based on previous research. The results did show that the music condition had a 5% higher SBR rate than the control condition, however unlike the difference between the Paro and control conditions, this was not statistically significant. The music condition also had significantly increased stimulation and enjoyment levels than the control group. These results suggest that the music did beneficially impact stimulation and enjoyment, but the power of the study was too low to detect effects on healing rates. The study was powered to detect a large effect size, and the effects of music on healing were small-medium compared to the control group. Further research could replicate this study with a larger sample size.

One possible explanation for why Paro was more effective at improving SBR rates than the music condition, is that the Paro robot is a combination of multiple types of EE, whereas

music only had the one auditory component. It has been proposed that combining multiple types of EE will result in better outcomes from their cumulative effects (Sale, 2018). Specifically, Paro may have been more effective as Paro provides social enrichment and increases companionship (Robinson et al., 2013). Social support has been found to improve SBR after a tape-stripping wound (Robinson, Ravikulan et al., 2017) and therefore, this social element may be a key factor. This could be due to the effect of oxytocin, a social bonding hormone. Vitalo and colleagues (2009) found that the beneficial effects of EE on burn healing in rats were similar to the effects of administering oxytocin. Other researchers have demonstrated that oxytocin can be induced via the skin activation from touch, and in particular stroking animals (Uvnäs-Moberg et al., 2015). Therefore, it may be that the pet-like companionship provided by Paro led to the release of oxytocin, which has been found to improve wound healing (Gouin et al., 2010). However, oxytocin was not measured in this study. Future research could further investigate the role of oxytocin.

Unlike music, the Paro robot was novel to the participants and this novelty aspect may have contributed to Paro's effects on SBR. However, previous research suggests that the effects of Paro persist over time and are not due to novelty. For example, one study found that the improvements in mood and reductions in depressive symptoms seen from the introduction of Paro to a rest home were still present over a year later (Wada et al., 2005). Other studies have shown that interaction with Paro actually increases and grows over time (W. Chang et al., 2013; Sabanovic et al., 2013). Future research could investigate whether the beneficial effects of Paro on SBR still occur in individuals already familiar with Paro.

It was hypothesised that differences in stress would mediate the relationship between condition and SBR. Although the subjective and objective stress measures showed the expected changes across the experiment, with an increase in self-reported stress and BP, and decrease in relaxation after the stressor, and a decrease in self-reported stress, BP, sCort and

sAA and increase in relaxation after the intervention, there were no differences between conditions. Therefore, in contrast to our hypothesis, stress could not be a mediator. This is in contrast with previous literature which has demonstrated that both music and Paro can decrease subjective and objective stress measures (Khalfa et al., 2003; McGlynn et al., 2016; Nomura & Hoshina, 2017). Therefore, Paro may have improved wound healing through a different mechanism.

Exploratory mediational analysis demonstrated that enjoyment significantly mediated the relationship between condition and SBR, indicating that the Paro condition had improved SBR at least partially due to enjoyment. This finding is supported by research which demonstrates that positive states such as happiness (Steptoe et al., 2005), optimism (Rasmussen et al., 2009) and positive affect (Cohen & Pressman, 2006) are associated with better health outcomes, including improved immune function. In particular, research has found that positive affect (Robles et al., 2009) and optimism (Ebrecht et al., 2004) are associated with improved wound healing, and therefore enjoyment could have a similar effect. Enjoyment, however, is less researched than other positive states, so less is known about its effects. One study found that Japanese men with higher life enjoyment had a lower risk of cardiovascular disease later in life, so enjoyment may be a protective factor (Shirai et al., 2009). Enjoyment of social activities has also been linked to better cognitive health in older adults, and this is proposed to be because enjoyment increases motivation and participation in activities (Flatt & Hughes, 2013). However, more research is required to further explore the effects of enjoyment on wound healing.

Limitations of the study are that the sample was relatively young, limiting generalisability to older people who are most at risk of poor healing. The unequal sex distribution of the sample may have also limited the results as males and females differ in their stress responsiveness. Also, the study had limited ecological validity as it was performed with an

experimental wound, in a laboratory setting and with experimentally produced stress. Future research should examine the effects of EE in more naturalistic settings and with clinical populations. Using the modified version of the TSST may have led to a less significant impact on physiological stress, so that little effects on sCort or sAA were observed. Future research could use the original TSST paradigm and add more sampling time points.

In conclusion, interacting with a Paro robot after a laboratory stressor led to improvements in SBR from an experimental tape-stripping wound and this effect was mediated by enjoyment. Future research is needed to corroborate this finding and its mechanisms in clinical populations.

Chapter 5- The Effects of Paro Robot in Patients with Psoriasis: A Pilot Study.

5.1 Preface

The first two studies in this thesis were conducted in healthy populations, to remove possible confounders with comorbidities that may affect wound healing rates. However, research in healthy populations is not clinically relevant or generalisable to populations who are at risk from complications from delayed wound healing. Also, the two studies had relatively young samples, which limits the ability to generalise the findings to older adults, who have impaired immune systems and therefore impaired wound healing processes. It is therefore important to examine if these effects extrapolate to a clinical patient sample.

Consequently, Study 3 examined the effects of interacting with the Paro robot on skin outcomes and stress in patients with psoriasis. Psoriasis is a common inflammatory skin disorder characterized by red scaly plaques on the skin (Griffiths & Barker, 2007). Psoriasis and skin healing share many similar skin processes and both largely rely on the function of the immune system (Morhenn et al., 2013). The barrier function of patients with psoriasis is impaired, drawing parallels with the SBR outcome used in the previous two studies (Leroy et al., 2015). Therefore, interventions, such as EE, that improve skin healing, and in particular SBR, may also be able to improve psoriasis clearance.

Furthermore, psoriasis has been found to be affected by psychological factors, especially stress. Reviews on the topic have found that there are relationships between measures of stress and the onset, recurrence and severity of psoriasis symptoms (Snast et al., 2018; Stewart et al., 2018). In addition, various psychological interventions have been found to improve psoriasis outcomes (Lavda et al., 2012; Xiao et al., 2019). Therefore, Study 3 used

the Paro robot as a possible short-term intervention to improve skin outcomes in psoriasis patients after a stressor.

Although previous studies have used the tape-stripping procedure on patients with psoriasis (Goon et al., 2004), it was decided to not conduct this procedure in the current study due to the risk of the Koebner phenomenon. This phenomenon describes the appearance of psoriatic lesions on non-involved skin, due to injury or trauma (Weiss et al., 2002). This can occur after even simple injuries such as tattoos or scratches. Studies have shown that tape-stripping can lead to the Koebner phenomenon in some patients with psoriasis (Raychaudhuri et al., 2008), and thus tape-stripping was not conducted in this study to minimise this potential risk. Therefore, this study used other measures of skin composition to examine possible changes due to interaction with Paro.

A novel addition to the literature was the use of Raman spectroscopy to examine possible short-term changes in the skin after the TSST and Paro. Raman spectroscopy is a technique that measures the biomolecular composition of the skin by using a laser to measure the light that is inelastically scattered by the different vibrational frequencies of molecules. This technique enables measurement of any changes in the composition of the skin. Although this technique has been used to reliably measure changes in the skin over time, no research has been conducted using Raman spectroscopy to measure acute changes in the skin due to psychological factors such as stress and enrichment.

Therefore, this manuscript aimed to investigate whether interacting with Paro could improve skin outcomes, measured via TEWL and Raman spectroscopy, and decrease psychological stress, after exposure to a stressor in patients with psoriasis. Originally, this study was planned to be a full randomised trial, consisting of a powered sample of 76 patients with psoriasis. However, due to difficulties with recruitment of this sample, combined with

COVID-19 restrictions, a sample size of only 25 patients was able to be obtained. Therefore, this study was resolved as a pilot study, with recommendations for future research to conduct a more powered trial to further examine the findings.

5.1.1 Citation

Law, M., Jarrett, P., Nieuwoudt, M. K., Holtkamp, H., Giglio, C., & Broadbent, E. (in submission). The effects of Paro robot in patients with psoriasis: A pilot study.

5.2 Introduction

Psoriasis is a common, chronic inflammatory skin condition that is characterised by red, scaly plaques that predominantly affect the elbows, knees and scalp, with a worldwide prevalence of approximately 1-2% (Griffiths & Barker, 2007). The plaques develop due to a hyperproliferation of keratinocytes and upregulation of inflammatory cytokines in the skin (Buske-Kirschbaum et al., 2007; Chapman & Moynihan, 2009). Patients with psoriasis have an accelerated rate of epidermal cell reproduction and therefore impaired skin barrier function (Maddock et al., 2019). Psoriasis may not be stable and patients can experience variability in its severity, with periods of remission or exacerbation through their life (O'Leary et al., 2004).

Patients with psoriasis may have substantial psychiatric comorbidities, which can significantly impair their quality of life. Psoriasis causes high levels of psychological distress and is associated with higher than normal rates of clinical depression and anxiety (Fortune et al., 2000; Kotrulja et al., 2010). Social embarrassment, isolation, rejection and poor body image are also common, as psoriasis is a visible and therefore stigmatising condition (Bundy et al., 2013). This level of stigmatisation strongly affects mental health. Psoriasis can therefore negatively affect psychological, vocational, social and physical functioning, making it imperative to improve the disease and symptoms to minimise these adverse effects (Shah & Bewley, 2014).

Although the aetiology of psoriasis is unclear, both genetic and environmental factors play a role (Heller et al., 2011). Both observational and experimental studies demonstrate that stress may play a critical role in the onset and exacerbation of psoriasis and stress can impede the success of treatments (Fortune et al., 2003; Stewart et al., 2018; Verhoeven et al., 2009). It is a cycle, as stress can worsen psoriasis and in turn, stress is also a consequence of psoriasis (Heller et al., 2011). This is particularly true for a subset of patients who believe

that stress affects their psoriasis. These patients are termed stress responders and they have been found to have different physiological responses to stress that can in turn cause exacerbations (Fordham et al., 2013; Zachariae et al., 2004). Although the role of the HPA axis and cortisol have been implicated, the exact mechanisms for the relationship between psoriasis and stress are yet to be fully elucidated (Stewart et al., 2018; Yang & Zheng, 2019).

Psychological interventions to reduce stress may be beneficial for clinical outcomes and quality of life. Many studies have shown promising results, including positive results for: psychotherapy (Price et al., 1991; Zachariae et al., 1996), cognitive behavioural therapy (Fortune et al., 2002; Piaserico et al., 2016; Sijercic et al., 2020), hypnosis (Tausk & Whitmore, 1999), emotional disclosure (Paradisi et al., 2010; Vedhara et al., 2007), mindfulness based cognitive therapy (Fordham et al., 2015; Maddock et al., 2019), relaxation (Neerackal et al., 2020) and mindfulness meditation (Kabat-Zinn et al., 1998). A meta-analysis showed that overall, psychological interventions had a medium effect on the reduction in psoriasis severity (Lavda et al., 2012). Further evidence demonstrates that these interventions may be particularly effective for those with high levels of stress and more severe psychiatric diagnoses (Sijercic et al., 2020). Even if psychological interventions do not directly affect psoriasis severity, they can have substantial impacts on patients' quality of life and psychological health (O'Leary et al., 2004; Zill et al., 2018).

Despite this promising evidence, many of these studies have important methodological limitations such as small sample sizes, lack of comparator groups and randomisation, no follow-ups, and high attrition rates and missing data (Chen et al., 2014; Lavda et al., 2012; Moon et al., 2013; Qureshi et al., 2019). In addition, most of these interventions are long-term (weeks to months) and therefore intensive for patients. Furthermore, clinical interventions usually require highly trained professionals. Few studies have investigated

whether brief psychological interventions that do not rely on specialist delivery could also improve psoriasis.

One type of brief intervention that could be beneficial is the companion robot Paro. Paro is a robot designed to resemble a baby harp seal and provide comfort to users like a pet. Using sensors, Paro proactively and reactively responds to the user's touch and voice through movements and noises (Wada et al., 2005). Paro also has a soft fur coat that provides tactile comfort when stroked. Interacting with Paro stimulates the user's senses and evokes emotions through social bonding (Shibata & Coughlin, 2014). Research has shown that Paro can reduce perceived stress (McGlynn et al., 2016), stress hormone levels (Nomura & Hoshina, 2017; Saito et al., 2003), loneliness (Robinson et al., 2013), depressive symptoms (C. C. Bennett et al., 2017), pain (Geva et al., 2020), and BP (Robinson, MacDonald et al., 2015), and improve mood (Inoue et al., 2013). Another study has found that interacting with the Paro robot for only 30 minutes can improve skin healing rates from an experimental tape-stripping wound after a stressor in people with healthy skin (Law, Jarrett et al., 2020b). This study indicated that there are direct benefits to skin healing by interacting with Paro. It was postulated that Paro may also be beneficial for patients with psoriasis.

The current study aimed to investigate whether interaction with Paro could decrease psychological stress and improve skin outcomes, measured via TEWL and Raman spectroscopy, after exposure to an experimental stressor in patients with psoriasis.

TEWL indicates the ability of the skin to prevent water loss through the epidermis. A higher TEWL value indicates a higher amount of water is evaporating through the epidermis and a lower skin barrier function. TEWL is higher in psoriasis plaques compared to non-affected skin and rises with increased severity, indicating impaired barrier function (Rajka & Thune, 1976). Therefore, TEWL can provide a measure of psoriasis severity.

Raman spectroscopy measures the vibrational frequencies of molecules, and thus is sensitive to changes in the molecular composition of skin areas affected by psoriasis. In this technique a small area of the skin surface is irradiated with a low power laser via a fibre optic probe. The light that is scattered inelastically by the biomolecules comprising the skin components is collected through the probe and analysed using a spectrometer. The measurement is non-invasive, non-painful and rapid; each measurement takes 20 seconds. Raman spectroscopy has previously been investigated for distinguishing between benign and cancerous tissue in a variety of organs including skin (Zhao et al., 2015), lung (Huang et al., 2003), larynx (Stone et al., 2000), prostate, gastric (Ouyang et al., 2015), colorectal (Li et al., 2014) and breast tissue (Vargas-Obieta et al., 2016).

It was hypothesised that after a stressor, all participants would have increased psychological stress levels and negative affect, and worsened skin outcomes including increased TEWL and increased levels of stress-induced biomarkers, compared with baseline levels. It was also hypothesised that those participants provided with Paro after the stressor will have improved positive affect and skin outcomes, with a reduction in the levels of stress-induced biomarkers in the psoriasis lesions, stress and negative affect levels, compared to the control condition, which was not provided with the Paro robot.

5.3 Method

5.3.1 Design

A 3(time-point) x 2(condition) mixed factorial randomised trial was designed to assess the effects of Paro vs. a control condition on skin outcomes and psychological variables after a stressor.

5.3.2 Sample

A sample of 25 adults with psoriasis (13 female, 12 male; average age= 43.00 years; range= 17-75 years) was recruited from the community using flyers, social media and email advertisements. Participants were included if they were over the age of 16, were diagnosed with plaque psoriasis and spoke fluent English. Participants were excluded if they had any other chronic skin conditions, were taking any systemic therapy for their psoriasis (including cyclosporin, methotrexate, acitretin, or concurrent phototherapy or biologic agents), were taking any other immunosuppressive medications (e.g. systemic corticosteroids) or had any recent or anticipated changes in anti-depressant or anxiolytic medications.

Ethics approval was granted by the University of Auckland Human Participants Ethics Committee.

5.3.2.1 Power Analysis. The required sample size was calculated using the programme G*Power (Faul et al., 2007) for a 2(conditions) x 3(time-points) mixed ANOVA. A power level of .80 and alpha level of .05 were chosen. An expected effect size of F= 0.29 was estimated from Law, Jarrett and colleagues (2020b) (gave N=64). The sample size was increased by 20% due to the possible errors in TEWL measurement, giving a total required sample size of 76. However, due to recruitment issues with the sample, alongside COVID-19 lockdown restrictions, recruitment for this study had to be ceased after only 25 participants. Therefore, this study can only be considered as a pilot study and proof of methodology, but is not powered to detect effects. The analysis of preliminary effects and the feasibility of the method is reported to inform further work.

5.3.3 Procedure

The study procedure is provided Figure 7. Interested participants first attended a 20-minute screening session with a dermatologist to assess their eligibility. After providing

informed consent, the dermatologist assessed the participants' skin to confirm the diagnosis of chronic plaque psoriasis and screened them for the other eligibility criteria. If the participant met all criteria, the dermatologist then completed the Psoriasis Area and Severity Index (PASI) (Fredriksson & Pettersson, 1978) which is a validated and accepted measure of overall psoriasis severity. The PASI uses a formula to combine estimates of the percentage of area of skin involved, with scores for the three main clinical manifestations of psoriasis (erythema, induration and desquamation) to get a score ranging from 0 to 72. Lastly, the dermatologist selected one psoriasis plaque to be used in the experimental session. The participants were asked to refrain from treating this selected plaque with any topical treatments or moisturisers until after the experimental session.

The second 90-minute experimental session then occurred at least one week after the screening session. A dehumidifier was running in the room to minimise possible confounds in TEWL measurements due to high ambient humidity. To start the experimental session participants completed baseline measurements including a questionnaire assessing demographics, health behaviours, questions about their psoriasis and psychological measurements. Participants were then asked to lie on a bed and expose the selected plaque. The researcher marked out two $1cm^2$ measurement areas; one on the selected plaque (the psoriasis site), and the other on uninvolved skin at least 1cm away from the plaque (the control site). The researcher then measured each of these sites using the Tewameter to assess TEWL, and the Raman spectroscopy to assess the composition of the skin.

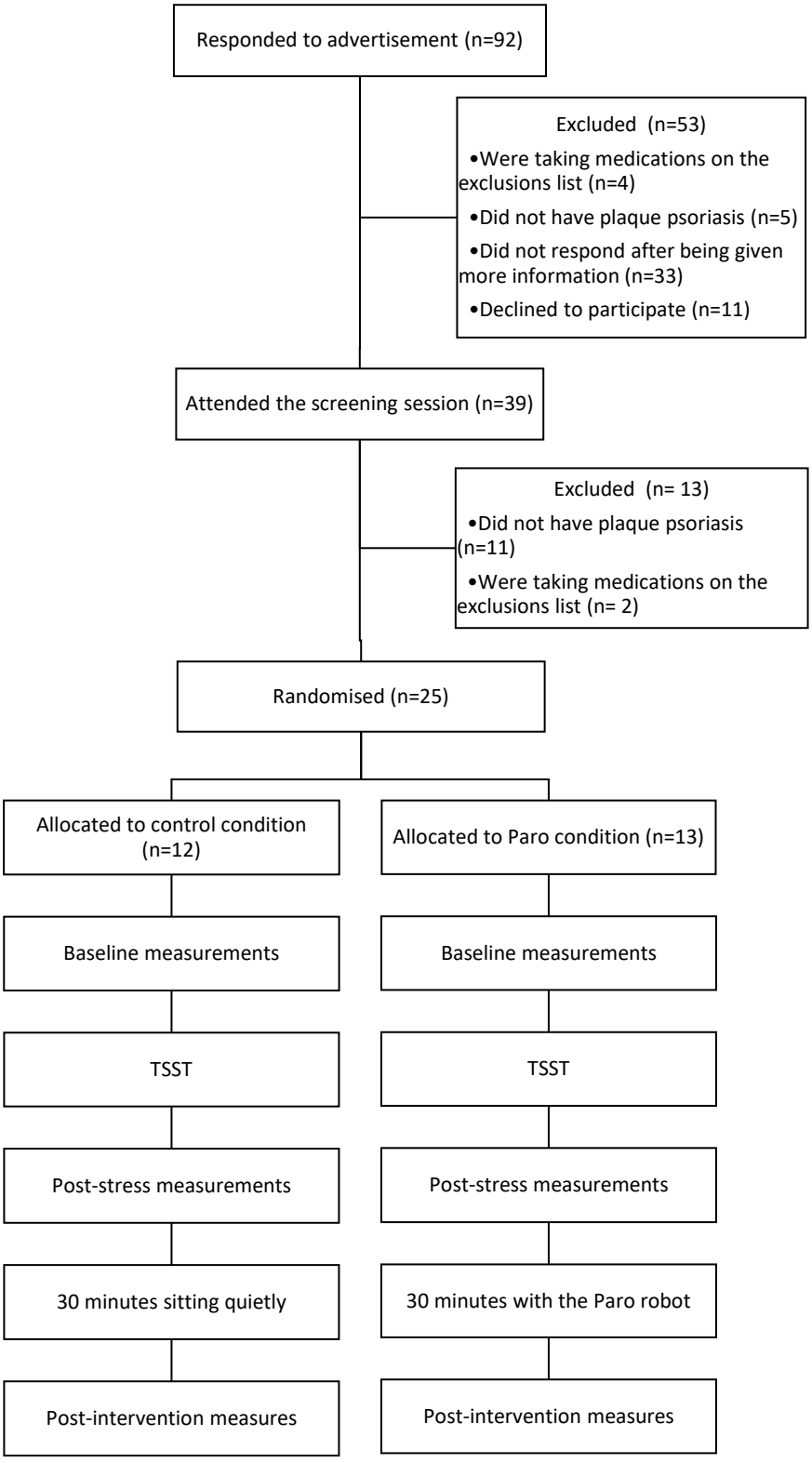


Figure 7. Overview of the study procedure.

After these measurements, the participants were exposed to a shortened version of the TSST to elicit stress (Kirschbaum et al., 1993). This task has been shown to reliably induce both physiological and psychological stress in most people (R. Miller & Kirschbaum, 2013). Participants were given three minutes to prepare and five minutes to present an oral speech on why they deserve their dream job. They were told that their speech would be video-recorded and a panel of judges would review it and award the best speech with a $100 voucher. A shortened version of the TSST, with the inclusion of only the speech-task has been found to be just as effective in eliciting stress as the full version of the TSST (Goodman et al., 2017).

After the stressor, participants again completed measures of psychological variables, TEWL and Raman spectroscopy before being randomised to one of two conditions (Paro or control). Randomisation was conducted by a researcher uninvolved in the study using a random number generator. Group allocation was concealed to the lead researcher up until this point, where the researcher opened a sealed envelope which contained the participants' assigned condition. Participants were asked to interact with the Paro robot (Paro condition) or to sit quietly (control condition) during the 30-minute intervention period, while they recovered from the stressor. Participants were asked not to use any personal electronic devices, scratch the selected plaque or fall asleep during this period. The researcher left the room and returned once 30-minutes had elapsed. All measures were then completed for a final time and participants were provided with a $40 voucher at the completion of the session.

5.3.4 Measures

5.3.4.1 Demographics and health behaviours. At baseline, participants were asked to report on their demographics including gender, age, weight, height and ethnicity. They were also asked to report on health behaviours including alcohol consumption (indexed as on average,

how many standard drinks they had per week), exercise levels (on average, how many days a week they engage in 30 minutes or more of physical activity), the quality of their diet over the past week from 1(very poor) to 5(very good) and on average, how many hours of sleep they had per night.

5.3.4.2 Psoriasis-specific questions. At baseline, participants were asked to answer questions about their psoriasis including the age they experienced their first outbreak and how many years they had psoriasis. They were also asked to state whether they believed that stress frequently worsens the severity of their psoriasis, with answers including yes, no and unsure. Lastly, they were asked to put a cross on a 100mm visual analogue scale to represent how severe they believed their psoriasis was right now. The anchors on the scale were no symptoms to worst symptoms imaginable.

5.3.4.3 Perceived stress. The 10 item PSS (Cohen et al., 1994) was used to evaluate the extent to which participants viewed their life as being stressful. Participants were asked how much they had felt a certain way over the last month on a scale of 0(never) to 4(very often). Scores were totalled to give a perceived stress score ranging from 0 to 40.

5.3.4.4 Depression. The Patient Health Questionnaire-9 (PHQ-9) (Spitzer et al., 1999) was used to measure depression levels at baseline. Participants were asked over the last two weeks, how often they had been bothered by a set of problems congregated from the DSM-IV depression criteria on a scale of 0(not at all) to 3(nearly every day). Scores were totalled to give a depression score ranging from 0 to 27.

5.3.4.5 Affect. Affect levels were measured at baseline, after the stressor and after the intervention period using the Positive and Negative Affect Schedule (PANAS) (Watson et al., 1988). This scale consists of two 10-item scales, measuring current positive and negative

affect levels. Participants were asked to rate the extent they felt certain emotions right now, on a scale of 1(not at all) to 5(very much). The scores for each scale were totalled to give a score for both positive affect and negative affect ranging from 10 to 50.

5.3.4.6 Visual analogue scales. Self-reported stress, relaxation and stimulation were measured at baseline, after the stressor and after the intervention period using 100mm visual analogue scales. Participants were asked to place a cross on a 100mm line to indicate how they were currently feeling. The anchors on the scales were not at all stressed to extremely stressed; not at all relaxed to very relaxed; and very bored to very stimulated. These visual analogue scales have been used successfully in previous research (Law, Jarrett et al., 2020a; Law, Jarrett et al., 2020b).

5.3.4.7 TEWL. TEWL was measured at the two sites, at three time-points (baseline, after the stressor and after the intervention period) using a Tewameter TM300 probe (Courage + Khazaka, Germany), which measures the evaporation rate (in $g/m^2/h$) in the air layer adjacent to the skin (Meesters et al., 2018). Before the measurements, the Tewameter probe was heated to 34°C by a probe heater to ensure it was at skin temperature. Once heated, the probe was placed against each of the two marked sites, measuring each site for 60 seconds, with one measurement being taken every second. 20 consecutive measurements with a standard deviation below 0.5 were averaged to give an overall TEWL value for both the psoriasis and control sites for each of the three time-points.

5.3.4.8 Raman spectroscopy. Raman spectra were recorded in vivo from participants at baseline, after the stressor and after the intervention period. Spectra were recorded using an EmVision Raman fibre optic probe and EmVision spectrometer, equipped with 1800 g/mm grating, a TEC CCD detector, 50 µm slit width and using 830 nm excitation at 40 mW. Five repeat spectra were recorded for 10-20 seconds from a 1.2 mm area on the skin of the 25

participants in each of the three time-points, from both the psoriasis and control sites, resulting in 375 spectra in total.

5.3.5 Statistical Analysis

The psychological and TEWL data were analysed using IBM SPSS Statistics 26. Mixed factorial ANOVAs were conducted to analyse the interaction and main effects of time-point and condition on the TEWL data and the psychological variables, including the visual analogue scales and the PANAS.

The Raman spectra were processed using an in-house Matlab algorithm to remove the fibre optic interference signal, and baseline corrected using a penalised asymmetric least squares algorithm (Eilers, 2003), after which the spectra were normalized to the peak position at 1436cm^{-1}. Principal component analysis (PCA) and ANOVAs were performed using MATAB and PLS Toolbox 8.1 (EigenVector technologies).

5.4 Results

5.4.1 Baseline Characteristics

The baseline and demographic characteristics for the sample are shown in Table 6; no significant differences were found between conditions. As shown in Table 6, on average the sample had a dermatologist rated PASI of 6.84 which represents moderate psoriasis. However, this score ranged from 1.20 to 21.30, indicating a large range in psoriasis severity across the sample. Self-reported psoriasis severity, reported via a 100-point visual analogue scale, followed a similar pattern with a mean rating of 40.64 (range= 6.00 to 80.00). The dermatologist and self-reported psoriasis severity ratings were significantly correlated with a large effect size (r=.70, p<.001).

Table 6
Summary of Demographic and Baseline Characteristics across Conditions

Baseline variable	Control (n=12)	Paro (n=13)	Total (n=25)	p-value
Age (years), M(SD)	41.25(18.66)	44.62(19.62)	43.00(18.84)	.665[a]
Sex, n(%)				
Female	7(58%)	6(46%)	13(52%)	.543[b]
Male	5(42%)	7(54%)	12(48%)	
BMI, M(SD)	24.24(5.01)	27.29(5.79)	25.83(5.53)	.193[a]
Exercise (days/week), M(SD)	4.58(2.11)	3.23(2.45)	3.88(2.35)	.155[a]
Diet Quality, M(SD)	3.67(0.65)	3.46(0.78)	3.56(0.71)	.483[a]
Sleep (hours/night), M(SD)	7.11(1.05)	6.50(1.14)	6.79(1.12)	.179[a]
PSS, M(SD)	12.67(6.91)	13.15(4.18)	12.92(5.54)	.831[a]
PHQ-9, M(SD)	12.75(2.14)	13.54(2.90)	13.16(2.54)	.451[a]
Selected Psoriasis Location, n(%)				
Leg	5(42%)	1(8%)	6(24%)	.067[b]
Arm	2(16%)	7(54%)	9(36%)	
Torso	5(42%)	5(38%)	10(40%)	
PASI Score, M(SD)	7.26(5.70)	6.45(6.39)	6.84(5.95)	.743[a]
Self-reported Psoriasis Severity, M(SD)	36.33(22.54)	44.62(25.92)	40.64(24.22)	.405[a]
Age of Psoriasis Onset, n(%)				
0-13	3(25%)	3(23%)	6(24%)	.903[b]
14-19	3(25%)	5(38%)	8(32%)	
20-29	5(42%)	4(31%)	9(36%)	
Over 30	1(8%)	1(8%)	2(8%)	
Years with Psoriasis, n(%)				.257[b]
<5 years	2(17%)	0(0%)	2(8%)	
5-10 years	3(25%)	2(15%)	5(20%)	

10-20 years	1(8%)	4(31%)	5(20%)
<20 years	6(50%)	7(54%)	13(65%)

Note: M=Mean, SD= Standard deviation, %= percentage of participants in that category. P-value was calculated by independent samples T-Tests[a] and Chi-square tests[b]

On average, the sample had moderate depression. The depression score of the sample was higher than depression levels in the general population, in concurrence with the literature on depression levels for patients with psoriasis. However, the sample had an average perceived stress score similar to the general population, indicating that this sample was not particularly stressed.

5.4.2 TEWL

A paired samples T-test was conducted to examine whether there was a difference in TEWL between the psoriasis and control sites at baseline. As expected, the psoriasis site had significantly higher baseline TEWL (M=31.70, SD=9.81) than the control site (M=17.58, SD=4.41, $t_{(23)}$=6.85, p<.001), indicating an impaired skin barrier function in psoriatic plaques compared to non-affected skin.

Mixed ANOVAs were conducted for both the psoriasis and control sites to evaluate the effects of time-point and condition on TEWL. There were no significant main effects of time-point (control site; $F_{(2,35)}$=1.70, p=.201, η_p^2=.07, psoriasis site; $F_{(2,44)}$=1.86, p=.168, η_p^2=.08) or condition (control site; $F_{(2,35)}$=1.03, p=.351, η_p^2=.04, psoriasis site; $F_{(1,22)}$=0.21, p=.650, η_p^2=.01) for either site. However, the medium effect sizes for time-point for both sites suggest that with a larger sample size, these effects could become significant.

There were also no significant interaction effects for condition x time-point for either the control ($F_{(1,22)}$=1.40, p=.249, η_p^2=.06) or psoriasis sites ($F_{(2,44)}$=0.28, p=.753, η_p^2=.01). The summary statistics for these tests are provided in Tables 7 and 8. The medium effect size for the control site indicates that this interaction effect could be significant in a larger sample. As

shown in Table 8, this is trending in favour of lower TEWL for the Paro condition at the post-intervention time-point.

Table 7
Summary Statistics and Post-hoc Comparisons for the Outcomes across Time, Irrespective of Condition

Task		Baseline	Post-stressor	Post-intervention
TEWL	Control Site, M(SD)	17.58(4.41)	18.60(4.91)	17.65(3.62)
	Psoriasis Site, M(SD)	31.70(9.81)	32.40(9.00)	30.71(9.49)
Visual Analogue Scales	Stress, M(SD)	26.92(22.67) b*c*	41.44(27.42) a*c**	11.60(13.68) a*b**
	Relaxation, M(SD)	75.32(15.36) b*c*	52.92(28.94) a*c**	83.72(17.68) a*b**
	Stimulation, M(SD)	65.20(20.52) b*c*	77.68(16.01) a*c**	40.48(27.96) a*b**
PANAS	Positive Affect M(SD)	31.40(8.56) c*	32.40(8.54) c**	25.52(9.68) a*b**
	Negative Affect, M(SD)	13.44(5.44) b*c**	16.16(6.11) a*c**	11.32(3.79) a**b**

Note: a=different to baseline, b= different to post-stressor, c= different to post-intervention, *p<.05, **p<.001, M=Mean, SD= Standard deviation, TEWL= trans-epidermal water loss.

Table 8
Summary Statistics for the Outcomes at the Post-Intervention Time-point across Condition

Condition			Paro	Control
TEWL		Control Site, M(SD)	17.21(3.34)	18.09(3.97)
		Psoriasis Site, M(SD)	30.20(10.86)	31.21(8.36)
Visual Analogue	**Scales**	Stress, M(SD)	15.38(16.53)	7.50(8.66)
		Relaxation, M(SD)	77.31(20.32)	90.67(11.40)
		Stimulation, M(SD)	42.54(29.41)	38.25(27.42)
PANAS		Positive Affect M(SD)	25.15(8.44)	25.92(11.24)
		Negative Affect, M(SD)	12.00(5.20)	10.58(0.90)

Note: M=Mean, SD= Standard deviation, TEWL= tran-sepidermal water loss, there were no significant differences in any outcomes between conditions (all *p*s>0.5).

5.4.3 Visual Analogue Scales

Mixed ANOVAs showed main effects of time-point for all psychological variables; stress ($F_{(2,40)}$=14.92, p<.001, η_p^2=.39), relaxation ($F_{(1,21)}$=22.72, p<.001, η_p^2=.50) and stimulation ($F_{(1,21)}$=60.44, p<.001, η_p^2=.48), with large effect sizes. The post-hoc tests are provided in Table 7. Irrespective of condition, the stressor led to an increase in stress and stimulation levels, and a decrease in relaxation. The intervention period resulted in a decrease in stress and stimulation to below baseline levels and an increase in relaxation to above baseline levels. There were no significant main effects for condition or interaction effects for any of the psychological variables. The means across condition at the post-intervention time-point are shown in Table 8.

5.4.4 PANAS

Mixed ANOVAS showed main effects for time-point for both positive ($F_{(1,31)}$=15.12, p<.001, η_p^2=.40), and negative affect ($F_{(2,35)}$=26.46, p<.001, η_p^2=.53), with large effect sizes. The post-hoc tests are provided in Table 7. Irrespective of condition, the stressor led to an increase in negative affect, and the intervention led to a decrease in both positive and negative affect to below baseline levels. There were no significant main effects for condition or interaction effects. The means across condition for the post-intervention time-point are shown in Table 8.

5.4.5 Raman Spectroscopy

The 375 spectra recorded of the psoriasis and control sites from the 25 participants are shown in Figure 8, after removal of the fibre optic interference signal, baseline correction and normalization to the peak position at 1436cm^{-1}. Large variations in the relative peak intensities of the spectral peaks are evident. These variations are due mainly to differences in skin types, the different body areas analysed, and the compositional differences between the psoriasis and control sites.

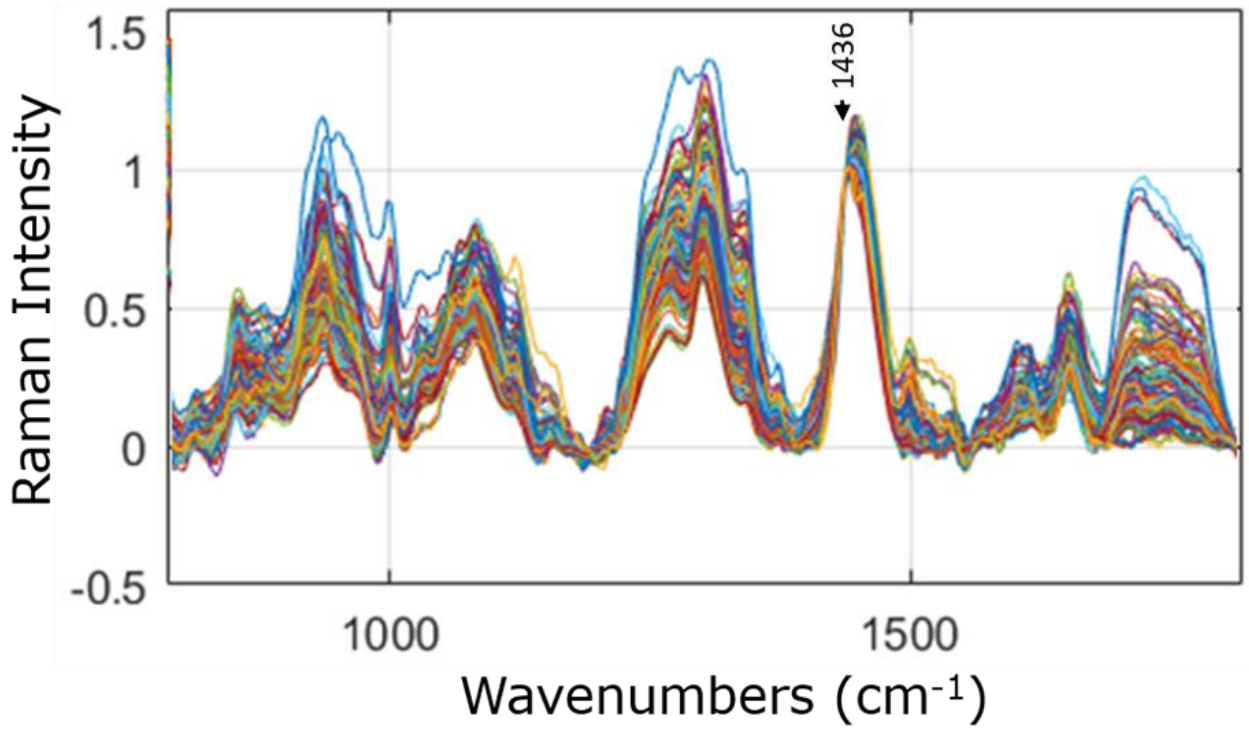


Figure 8. Raman spectra recorded of psoriasis and control sites from all 25 participants, overlaid for comparison and normalised to the peak height at 1436cm^{-1}, indicated by the arrow.

5.4.5.1 Analysis of the Raman spectra. The Raman spectra were analysed to investigate whether any changes in the molecular vibrations of the psoriasis regions had occurred over the three time-points. The five repeat spectra recorded at each time-point and site were averaged, and then the control site was subtracted from the psoriasis site, resulting in 75 difference spectra: three difference spectra for the three time-points, for each of the 25 participants.

A PCA of the 75 difference spectra between the psoriasis and control sites was performed (after mean-centering of the difference spectra to explore similarities or differences between the three time-points). 95% of the variance in the spectra was described by 12 principal components (PC's). No clear clustering of the sample scores according to the three time-points was evident. However, as a group most of the post-intervention time-point samples (blue) appear slightly more toward the left-hand side of the X axis in Figure 9a, which

indicates they have lower values for the positive loadings of the sixth PC (PC6). The adjacent loading plot in Figure 9b (bottom) indicates, for each wavenumber, the extent to which the scores are associated with that PC. The positive "peaks" in the loading plot for PC6 (red curve) represent those wavenumbers, and hence molecular species, that are affiliated more with the red post-stressor and green baseline time-point samples, while the blue post-intervention time-point sample scores appear on the negative side of PC6 in the PCA score plot (Figure 9a), with the higher loadings corresponding with wavenumbers between 820-1000cm^{-1} (Figure 9b).

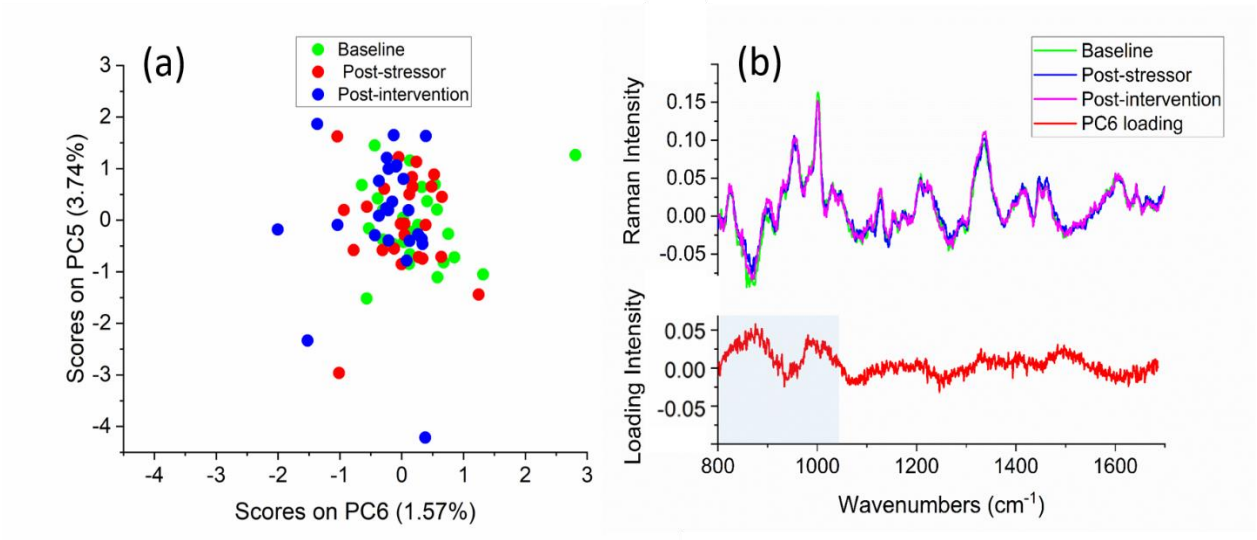


Figure 9. (a) PCA scores colour coded according to time session and (b) top: the averaged difference spectra (averaged psoriasis – averaged control) for each time-point (light green: baseline, blue: post-stressor, pink: post-intervention), (b) bottom: loading plot for PC6, with shaded region corresponding to positive loadings for this PC.

While the grouping of post-intervention scores on the negative side of PC6 accounts for only 5.3% of the total variance and around one third of the scores from each of baseline and post-stressor time-points also show higher negative loadings for these compounds, PC6 was the highest PC that showed grouping for any of the time-points (with PC1 being the highest loading overall). The scores for PCs 1 to 5 showed no grouping for the three time-points; the PC1 loadings represented the mean, accounting for differences in overall spectral intensities

between some of the individual participants from the others, while PC loadings 2, 3 and 4 showed differences mainly in the 1450cm^{-1} lipid region, amide I and III bands and phenylalanine band at 1003cm^{-1}, also for a few individuals only as indicated by the scores plots.

To test how significant the increased intensities in the difference spectra of the post-intervention time-point were compared to the baseline and post-stressor time-points, an ANOVA was performed on the band areas in the region 820-980cm^{-1} which displayed the highest negative loadings (marked in Figure 9b). There were no significant differences between any of the time-points; baseline and post-stressor (p=0.977, d=0.38), baseline and post-intervention (p=0.127, d=0.78) and post-stressor and post-intervention (p=.143, d=0.47).

A two-way ANOVA (time-point vs condition) of four main peak areas in the difference spectra was also performed on each of the areas of the peaks at 1340, 1001, 958 and 901cm^{-1} (labelled in the difference spectra shown in the lower plot Figure 9b) for the 25 difference spectra. No significant effects were found in these peak areas or peak area ratios, on any of these peak areas with time-points or between the Paro and control conditions.

5.5 Discussion

This randomised pilot study investigated the feasibility of interacting with a Paro robot after a stressor on skin outcomes and psychological variables in patients with psoriasis. Although the study was planned as a full randomised control trial, recruitment issues meant the study was completed as a pilot, and feasibility and effect sizes are reported to inform future research.

Significant effects of the experimental manipulations were seen, demonstrating feasibility of the experimental paradigm. The stress task significantly increased stress, stimulation and negative affect levels and decreased relaxation, in both conditions, as expected. The

intervention period, on the other hand, led to a decrease in stress, stimulation, negative affect and positive affect to below baseline levels, and an increase in relaxation to above baseline levels. This indicates that the method worked to induce stress and promote stress recovery.

TEWL was significantly different between the psoriasis and control sites, which was expected, and indicates that TEWL is a valid measure of psoriasis. There were no significant differences in TEWL across the experimental session or between conditions. However, effect sizes suggest that these effects could become significant in a fully powered sample, suggesting feasibility of this measure in larger trials. The Raman results indicated a trend towards differences across the time-points; however, no differences across conditions were found.

Although previous research has suggested that Paro can decrease stress (McGlynn et al., 2016; Nomura & Hoshina, 2017; Saito et al., 2003) and improve skin outcomes (Law, Jarrett et al., 2020b) no significant effects of condition were seen in this pilot study. This lack of effects could be due to a variety of reasons. Most importantly, the study was not powered to detect any intervention effects. The effect size for the TEWL measurements between conditions in the non-psoriatic skin suggests that a significant effect may be detected in a larger sample of at least 114 participants.

As well as the low sample size, there was large individual variability in the sample. Research has demonstrated that psychological interventions may be more beneficial for certain patients. For example, a recent meta-analysis demonstrated that effect sizes from cognitive-behavioural interventions for patients with psoriasis were highest in those patients with higher psychopathology pre-treatment (Sijercic et al., 2020). The current sample had a wide range of depression and stress scores. Therefore, it may be that Paro is only effective for those with higher depression and stress. Paro may be less effective for those who are already

psychologically adaptive. The meta-analysis also found that effect sizes were larger for those with more severe psoriasis (Sijercic et al., 2020). The patients in the current study had PASI scores ranging from very mild to very severe; however, many only had mild psoriasis, as is common in the wider community. Psoriasis may be less psychologically damaging to those with lower PASI scores, especially if it can easily be hidden. Therefore, the psychological and stress-reducing effects of Paro may be more effective in those with more severe psoriasis.

Lastly, the literature demonstrates that patients with psoriasis have differences in stress-reactivity (Zachariae et al., 2004). Although stress may trigger flare-ups in stress-responders, this may not be seen in non-stress responders, and therefore psychological interventions to reduce stress may not be effective in these patients (Fordham et al., 2013). The current study did ask participants to report whether they believed stress worsened their psoriasis; however, there were only 16 stress-responders and one non stress-responder, with the rest of the sample reporting that they were unsure. Therefore, the recruitment of only stress-responders may lead to stronger effects. Despite these propositions about individual variability effects, the sample size for this study was too small to complete any sub-analyses on these possible individual factors. Future research should ensure a large enough sample to be able to examine these possibilities.

Another possible explanation for the null results of condition could be the brief time-frame of the intervention. A one-off 30-minute intervention may not be long enough to see significant biological changes in the skin that could be measured by Raman spectroscopy, especially for psoriasis, which is a chronic and long-term disease. The physiological stress response is an evolutionarily mechanism which induces a rapid response in the face of a threat. Therefore, an acute change in physiology would be expected, but may not have been significantly detected by the Raman technique. Previous research on psychological interventions for psoriasis tend to use longer interventions ranging from weeks to months.

This study attempted to investigate whether a short-term intervention could have a similar benefit; however, the lack of effects may indicate that this is not possible. Raman spectroscopy has also not been previously used in short-term studies to investigate acute changes in the skin from psychological factors. Future research could therefore investigate the effects of Paro on psoriasis outcomes over a long-term study in order to detect any significant changes in psoriasis severity over time.

Despite the lack of significant effects between conditions, this study did demonstrate significant changes in the outcomes over the experiment, therefore indicating the feasibility of the experimental paradigm for future research. Even with a limited sample size, this study showed that the stress task was successful at changing the participants' mood and stress levels and in contrast, the intervention period allowed for successful stress-reduction to below basal levels. Therefore, this paradigm is successful at changing short-term psychological outcomes in patients with psoriasis. However, stress induction and recovery were observed in both conditions and therefore, the TSST may have been too stressful to observe any significant intervention effects. Future research may investigate this intervention in patients experiencing more naturalistic stressors.

The Raman analysis was also seen to be feasible. The lower PCA scores as a group of the post-intervention time-point difference spectra for the positive loadings for PC6 suggest that the psoriasis sites after the intervention showed differences in the vibrational energies of the biomolecules from the baseline and post-stressor time-points. This band region includes the C-C ring stretching vibrations of a number of amino acids, which in skin would be primarily proline, hydroxyproline (Erckens et al., 1997; Parker, 1983; Talari et al., 2015), tyrosine and tryptophan (Hernández et al., 2016; Talari et al., 2015). The latter two compounds are among the cytokines which are increased in inflammatory skin conditions (de la O-Cuevas et al., 2019; Portugal-Cohen et al., 2012). Although none of the effects of time-point on the loading

areas in this region were significant, the *p*-values close to 0.1 between baseline and post-intervention, and between post-stressor and post-intervention support the preference for this region of post-intervention scores. The medium to large effect size of PC6 score between the baseline and post-intervention time-points shows that the intervention period, in both conditions, reduced proteins associated with cytokines that are increased in inflammatory skin conditions such as psoriasis, from baseline level. This is an important finding as reducing these pro-inflammatory cytokines can lead to a reduction in psoriasis severity and symptoms.

The strict eligibility criteria for the study led to low recruitment and the exclusion of many patients with psoriasis. For example, the study protocol excluded participants on any form of systemic therapy or immunosuppressive medication for psoriasis to minimise a confounding effect. These criteria were made clear on any advertisements and therefore, these patients may not have approached the researchers. This may have limited the sample of the study to only participants with milder psoriasis, as those with severe psoriasis are more likely to be on systemic treatment. Future research should include these patients as well to further expand the sample and improve recruitment rates.

In conclusion, this pilot study did not significantly demonstrate that interacting with a Paro robot after a stressor could influence skin outcomes or psychological variables in patients with psoriasis compared to a control condition, who did not receive a Paro robot. However, effect sizes for both the TEWL and Raman measurements suggest feasibility for a larger study that may be able to find significant effects across conditions. This pilot study also indicates the feasibility of the experimental methodology, as expected significant findings with medium effect sizes were observed from the experimental manipulations. Future research should investigate this work in larger samples of people who are experiencing significant stress, with sub-group analyses using a longer-term intervention period.

Chapter 6- Viewing Landscapes is More Stimulating than Scrambled Images after a Stressor: A Cross-Disciplinary Approach

6.1 Preface

Visual enrichment is another important form of sensory EE. Visual EE is one of the easier forms of EE to incorporate into humans' everyday lives, as it can involve adding simple interventions (such as pictures, videos, artworks, colours and nature) into the environment. The second theme of this thesis investigated the use of artwork as a possible EE for humans to reduce stress outcomes. In particular for this manuscript, nature artworks were used as a form of visual EE.

Nature itself is a form of EE, which has been found in many studies to reduce levels of psychological (Olafsdottir et al., 2018; Ulrich, 1979) and physiological (Brown et al., 2013; Hunter et al., 2019) stress. However, direct access to nature is not always feasible or attainable. Growing evidence is demonstrating that viewing representations of nature through landscape artworks can lead to similar effects from that of viewing real nature. This suggests an alternative and more easily accessible option to provide nature as EE.

This pilot study therefore aimed to use an interdisciplinary approach to investigate the effects of viewing landscape artworks on recovery after the TSST as a stressor. Landscape artworks were compared to scrambled versions of these artworks as a control condition. This study used multiple measures of recovery, to examine both the psychological and physiological stress responses to viewing landscapes. Participants' pupil sizes were also tracked while viewing the artworks in order to measure arousal and stimulation. This was to examine the possible mechanisms behind how viewing the artworks may reduce stress and improve recovery.

This study focused on whether viewing landscape artworks could improve stress outcomes and potential mechanisms but did not assess wound healing. It was important to first assess the protocol, images and timing of the experimental procedure before introducing wound healing as an outcome. If the preliminary research demonstrates that viewing landscapes can influence the stress response, then it can inform future wound healing research in this area.

6.1.1 Citation

Law, M., Minissale, G., Lambert, A., Nater, U. M., Skoluda, N., Ryckman, N., Tahara-Eckl, L., Bandzo, M., & Broadbent, E. (2020). Viewing landscapes is more stimulating than scrambled images after a stressor: A cross-disciplinary approach. *Frontiers in Psychology*, 10, 3092. https://doi.org/10.3389/fpsyg.2019.03092

6.2 Introduction

Throughout history, exposure to nature has been touted as restorative for health and research supports this proposition. Although nature is experienced in multi-sensory ways, research has focused on the effects of viewing nature on health, due to the dominance of vision in experiencing nature (Ulrich, 1981).

Viewing nature has been found to have effects on health in both healthy and patient populations. One review found that the effects of nature fall into three categories: short-term recovery from stress, recovery from illness and long-term improvements in mood (Velarde et al., 2007). Viewing nature, either live or through photographs and videos, has been linked with a wide range effects, including: increased relaxation as shown through EEG (C. Y. Chang, 2002), decreased anxiety about surgery (Ulrich et al., 1993), increased heart rate variability (HRV) (Gladwell et al., 2012), decreased job stress, increased life satisfaction (Kaplan et al., 1988) and decreased pain (M. P. White et al., 2019). A recent study by White and colleagues (2019) found that the optimal dose for improved health and wellbeing was 120 hours of nature contact per week; however, the beneficial effects of nature have been found to occur within less than five minutes (Ulrich, 1992).

Research has also shown that nature has a restorative effect on the stress response. Stressed individuals report improved mood after viewing nature scenes compared to viewing nothing or urban scenes (Ulrich, 1979). Nature can also improve physiological recovery from a stressor when viewed after (Ulrich et al., 1991) or before (Brown et al., 2013) experimental stressors. Lastly, nature has also been found to lower cortisol levels in both stressed and unstressed individuals (Hunter et al., 2019; Olafsdottir et al., 2018).

Three main theories have been proposed for the beneficial effects of viewing nature on health; evolutionary theory, attention restoration theory (ART) and nature as positive

distraction (Nanda et al., 2010). Evolutionary theory proposes that responses to nature are influenced by genetics (Kweon et al., 2008). As humans evolved in natural environments, we have an innate predisposition to experience restoration as a response to nature (Ulrich et al., 2003). As a consequence of our evolutionary heritage, natural environments are processed more efficiently, as our sensory, cognitive and emotional systems evolved in this landscape (Ulrich et al., 1991). Conversely, these systems are likely to function more poorly in artificially constructed, urban environments which are more recent phenomena. This theory explains why natural scenes are more beneficial to health than urban scenes.

ART postulates that stress causes mental fatigue which impacts cognitive processes. However, the restorative characteristics of nature can counteract this, resulting in better recovery from this mental fatigue (Kaplan, 1995). In this theory, nature is restorative because it is attention-grabbing and engaging, in a non-threatening way, and therefore reduces cognitive strain (Berman et al., 2008). ART therefore provides a possible explanation as to why people exposed to nature have reduced stress responses.

The last theory is that nature is a form of positive distraction. Positive distraction refers to an element of the environment that produces positive feeling and holds attention effortlessly. This attracts attention away from negative stimuli and experiences such as stress. Nature is effective as a positive distraction because it is stimulating and evokes interest and positive affect, allowing the displacement of negative affect (Hartig et al., 2011).

These three theories are not mutually exclusive. The attention system of the human brain (Petersen & Posner, 2012; Posner & Petersen, 1990) has a long evolutionary history (Graziano, 2014) and includes a range of processes, which include focusing attention, managing cognitive resources, and responding to distractions. Research to date shows strong evidence that viewing nature is beneficial to health and aids in stress recovery. There is also

growing evidence indicating that representations of nature through artwork can have similar effects through the same mechanisms (Ulrich et al., 2006).

Artworks that depict nature scenes have increasingly been used in research and healthcare settings to reduce stress and improve health. Research demonstrates that, like real views of nature, artwork can reduce anxiety (Binnie, 2010), reduce depression (Staricoff et al., 2003), improve mood (Karnik et al., 2014), increase relaxation (Wang et al., 2015) and decrease anxiety medication usage (Nanda et al., 2011), when compared to no artwork. This collection of studies demonstrates that nature artworks can significantly improve psychological wellbeing. However, some research shows null results. A recent study found that nature artworks did not improve mood, pain, anxiety, depression and satisfaction for chemotherapy patients (George et al., 2017). But in subsequent interviews, the patients reported the artwork provided a positive distraction from chemotherapy.

Although this evidence indicates that nature artworks have a positive effect on psychological health, there is a scarcity of evidence for the effects of these artworks on physiological outcomes. An early study by Heerwegen (1990) found that HR was lower for dental patients on the days where a landscape mural was hung in the waiting room compared to no mural. Mastandrea et al (2019) found that visiting art museums lowered systolic BP compared to visiting an office with no artworks; however, this study did not look specifically at artworks depicting nature. Therefore, more research is needed to determine whether experiencing nature artworks can improve physiological outcomes.

Most nature research has used urban scenes as a control. However, this approach has many confounding variables such as the degree of colour in the nature vs. urban scenes, as colour is an important mediator in the relationship between art and mood (Lankston et al., 2010). A more appropriate control is scrambled images, as used in previous research on the effects of

artwork on attention and memory (Wang et al., 2015). Scrambled images are edited versions of artworks which have been digitally disarranged. We propose these images act as better controls as they retain the colours and brightness of the original artwork, but the representation of nature is removed (Wang et al., 2015). This allows a better understanding of whether the depiction of nature in the art is the key factor in improving outcomes, rather than structural features.

The current pilot study used an interdisciplinary approach to investigate whether nature artworks can improve psychological and physiological recovery from a laboratory stressor, when compared to viewing scrambled images of the artworks. Stress responses were assessed using measures of: self-reported affect, fatigue and drowsiness, and sCort and sAA. Participants' pupil size was also measured while viewing the artworks to provide an indication of the degree of stimulation and arousal that the artworks provided.

In this pilot study, we investigated the feasibility of study procedures, as well as estimates of effect size. Based on prior research, it was hypothesised that viewing nature artworks after a laboratory stressor would lead to improved stress recovery, as indexed by decreased sCort, sAA, fatigue and drowsiness, improved affect levels and increased pupil size compared to the control condition who viewed scrambled images.

6.3 Materials and Methods

6.3.1 Sample

A sample of 30 adults (20 female, 10 male; average age 27.20 years, age range 18 to 52 years) was recruited from the community through flyers and email advertisements. Participants were included if they were over the age of 16 and spoke English. Ethics approval was granted by the University of Auckland Human Participants Ethics Committee.

6.3.2 Procedure

In accordance with salivary sampling procedures, participants were instructed not to chew gum or drink caffeine, juice or alcohol 18 hours prior to the study and not to eat or brush their teeth in the hour before their session. Prior to their laboratory session, participants were randomised to one of two conditions; control (scrambled images) or nature (landscape images). Randomisation was performed by a researcher uninvolved in the experiment using a random number generator. Randomisation was concealed until the start of the session, when the sealed envelope containing the group allocation was opened.

Participants attended a 90-minute experimental session and gave written informed consent. The procedure is shown in Figure 10. Baseline questionnaires about the participant's demographics and affect levels were completed, and the participant provided a saliva sample. Once baseline measures were taken, participants were exposed to a shortened version of the TSST (Kirschbaum et al., 1993). Participants were given three minutes to prepare and three minutes to present a speech to convince the experimenter to give them their dream job. Participants were told their speech would be recorded and a panel of judges would review it and award the best speech with a $100 voucher. A shortened version of the TSST was used as a recent meta-analysis has shown that the shortened version produces similar physiological stress responses to the full TSST paradigm (Goodman et al., 2017).

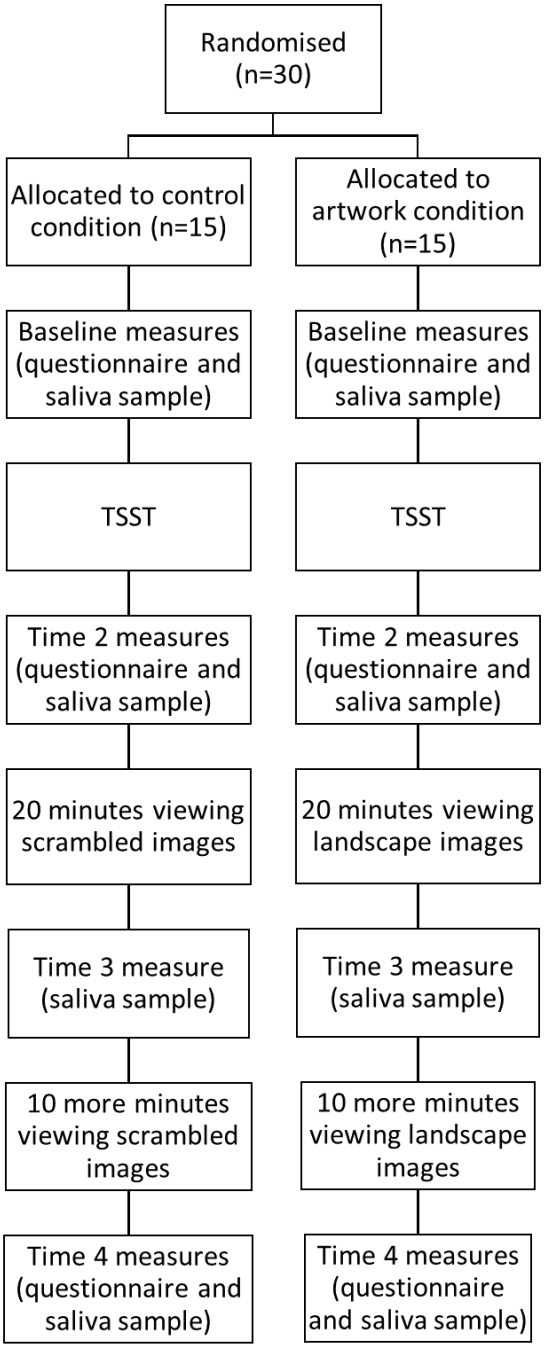


Figure 10. Flow chart showing the procedure of the study.

The participants then completed the affect measures and provided a saliva sample for a second time. They then viewed a 30-minute slide-show comprising of 26 images based on their random group allocation. Participants in the landscape condition were shown a set of landscape artworks by New Zealand artists. The landscapes were included if they contained a

nature scene that was relatively void of detailed focal points and non-natural stimuli. The scrambled condition viewed digitally scrambled versions of the landscape artworks, similar to work by Wang and colleagues (2015). A 2-dimensional Fast Fourier transform was performed on each image, in order to generate the scrambled version. These images no longer have any sense of "objectness", but they preserve the colour and luminance profiles of the original images. Examples of the original artworks and their scrambled versions are shown in Figure 11. Participants' pupil size was tracked during the viewing period.

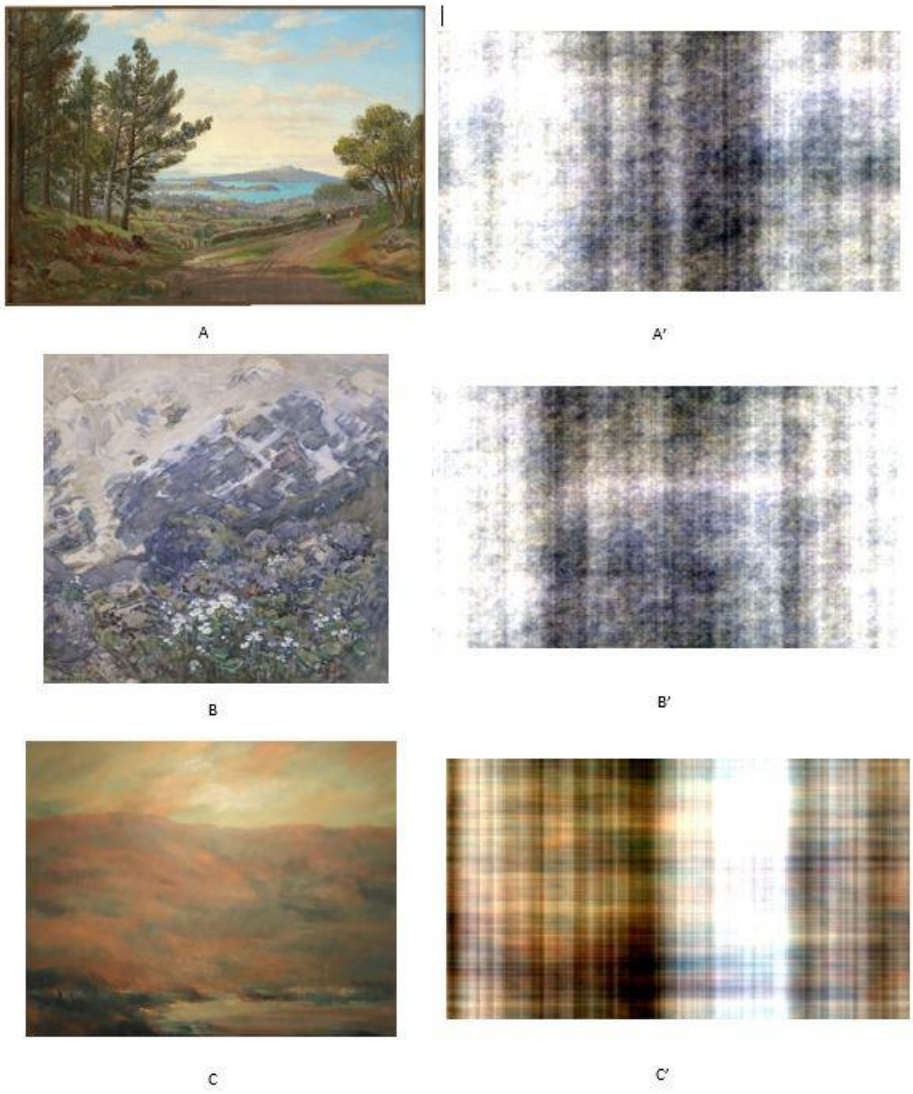


Figure 11. Examples of the landscape artworks (A, B, C) and their scrambled versions (A', B', C').

20 minutes into this viewing period, the researcher entered and asked the participant to provide another saliva sample. Participants viewed the images for a further 10 minutes before completing the final set of measurements. At the end of the session, participants were debriefed and received a $40 voucher for participation.

6.3.3 Measures

6.3.3.1 Demographics. At baseline participants were asked about their demographics including: gender, age, height, weight and ethnicity.

6.3.3.2 Affect. Affect levels were assessed at baseline, after the stressor and after the viewing period using a modified version of the Actual Affect Subscale of the Affect Valuation Index (AVI; J. L. Tsai et al., 2006). This scale consisted of a list of 25 emotions and participants were asked to rate how much they felt that emotion at that present moment on a scale of 1(not at all) to 5(extremely). These instructions were modified from the original scale which asked the participants to rate how they felt over a typical week. These modified instructions have been used successfully in previous studies (Nair et al., 2015; Robinson, Ravikulan et al., 2017).

Eight aggregate component scores were calculated: high arousal positive affect (HAP; strong, excited, enthusiastic), low arousal positive affect (LAP; calm, relaxed, rested, peaceful), positive affect (PA; happy, content, satisfied), negative affect (NA; sad, lonely, unhappy), high arousal negative affect (HAN; hostile, fearful, nervous), low arousal negative affect (LAN; dull, sleepy, sluggish), low arousal affect (LA: quiet, still, passive) and high arousal affect (HA; aroused, surprised, astonished). This scale is valid and reliable across different populations and each component score has high internal consistency (J. L. Tsai et al., 2006).

6.3.3.3 Fatigue and drowsiness. Participants were asked to rate how much they were feeling fatigue and drowsiness on a scale from 0(not present) to 3(severe) at baseline, after the stressor and after the viewing period (Petrie et al., 2014).

6.3.3.4 Salivary stress biomarkers. Saliva samples were collected at baseline, after the stressor, 20 minutes into the viewing period and after the viewing period as per protocol using SaliCaps collection device (IBL, Hamburg, Germany). These samples were taken to examine any changes in stress biomarkers (sCort and sAA) associated with the viewing and stress tasks (Strahler et al., 2017). Participants were asked to rinse their mouths with water, before collecting saliva using the passive drooling technique. Participants collected their naturally secreted saliva in their mouths for two minutes by not swallowing, before transferring the accumulated saliva to the SaliCap. The samples were stored at -20° C at the University of Auckland before they were shipped on dry ice to the University of Vienna, where they were biochemically analysed. Concentrations of sCort were measured using commercially available enzyme-linked immunosorbent assay (ELISA, IBL, Hamburg, Germany). sAA activity was determined using a kinetic colorimetric test (Strahler et al., 2016) using reagents obtained by Roche (Roche Diagnostics, Mannheim, Germany). Intra- and inter-assay coefficients of variance of both tests were below 10%.

6.3.3.5 Pupil size. Participants viewed digital versions of the artworks and scrambled images on a 23” monitor, controlled by a Dell Optiplex PC. Viewing distance from the screen was approximately 60cm, and changes in pupil size were monitored by an eye-tracker (the EyeTribe, Denmark). Participants rested their chin on a chin rest, to keep their heads still during the viewing period. During the first (20-minute) block of images, participants viewed 17 images in succession; in the second (10-minute) block of images, participants viewed nine images. Each trial began with presentation of a dark screen with white cross in the centre for

three seconds, followed by a uniform grey screen for four seconds, followed by an image (landscape or scrambled image) for 60 seconds. Participants were instructed to look at the white cross at the beginning of every trial. Following the disappearance of the cross, participants were free to move their eyes to explore the succeeding images. Each participant viewed a different random sequence of images, and allocation of images to trial blocks was counterbalanced.

6.3.4 Statistical Analysis

Data were analysed using IBM SPSS Statistics 22. Mixed factorial ANOVAs were completed to analyse the interaction and main effects of time-point (baseline, post-stressor, during artwork and post-artwork viewing) and condition (scrambled vs. landscape) on affect, sCort and sAA. ANCOVAs for changes in sCort and sAA controlling for baseline levels were conducted for the recovery period (from post-stressor to post-viewing period). The sCort and sAA data violated the assumption of normality and was transformed using a natural log transformation and logged values were used in the analyses. Mean pupil size data (in mm^2) were entered into a mixed factorial ANOVA with image (grey screen vs. image) and trial block (one vs. two) as within-subjects factors; group (landscape vs. scrambled) was the between-subjects factor.

All tests were reported using the Greenhouse-Geisser adjustment due to violations in sphericity (Vasey & Thayer, 1987). All significant interaction effects were followed up using simple pairwise comparisons with Bonferroni corrections.

6.4 Results

Baseline characteristics are given in Table 9. No significant differences between the two conditions were found.

Table 9

Summary of Demographics and Baseline Characteristic of Participants across Condition

Baseline variable	Scrambled	Landscape	p-value
Age (years), M(SD)	27.53(8.83)	26.87(5.41)	.805[a]
Gender (%)			.439[b]
Female	11(73%)	9(60%)	
Male	4(27%)	6(40%)	
Ethnicity (%)			1.000[b]
NZ European	6(60%)	6(60%)	
Non-European	9(40%)	9(40%)	
BMI, M(SD)	24.50(4.31)	25.28(4.70)	.640[a]
Exercise days/week, M(SD)	4.07(1.75)	4.00(2.20)	.928[a]
Baseline sCort (nmol/L), M(SD)	3.61(2.44)	4.01(5.15)	.778[a]
Baseline sAA (U/mL), M(SD)	81.92(99.00)	44.49(51.18)	.204[a]

Note: M=Mean, SD= Standard deviation, %= percentage of participants in that category. P-value was calculated by independent samples t-tests[a] and Chi-square tests[b]

6.4.1 Affect

No significant main effects were observed for the effect of condition on any of the eight AVI component scores (all *ps*>.05). Significant main effects of time-point were found for the following components: HAP ($F_{(2,53)}$=21.33, p<.001, η_p^2=.44), LAP ($F_{(2,46)}$=6.38, p=.006, η_p^2=.19), PA ($F_{(2,55)}$=3.96, p=.025, η_p^2=.12), HAN ($F_{(2,51)}$=6.46, p=.004, η_p^2=.19), LAN ($F_{(1,35)}$=19.49, p<.001, η_p^2=.41), LA ($F_{(2,53)}$=7.04, p=.002, η_p^2=.20), HA ($F_{(1,71)}$=4.62, p=.029, η_p^2=.14). Post-hoc tests indicated that irrespective of condition, the stressor caused PA and LAN to decrease, and the artwork viewing caused the low arousal affect components to

increase and high arousal affect components to decrease. Therefore, irrespective of condition, the stress and viewing tasks change participants' affect.

A significant interaction effect was observed on the LAN component ($F_{(1,35)}$=3.97, p=.045, η_p^2=.12). Follow-up tests for each time-point revealed that there were no significant differences in LAN across the conditions at any time-point (all ps>.05). However, the differences between conditions were approaching significance after the viewing period ($t_{(28)}$=1.85, p=.075) with the scrambled condition having higher LAN affect (M=8.33, SD=3.42) than the landscape condition (M=6.07, SD=3.31).

A significant interaction effect was also observed on the HA component ($F_{(1,37)}$=3.81, p=.048, η_p^2=.12). Follow-up tests revealed that there were no significant differences in HA across the conditions at any time-point (all ps>.05). No significant interaction effects were observed for any other components.

ANCOVAs on change scores of the AVI components from post-stressor to post-viewing period, controlling for post-stressor scores, are shown in Table 10. LAN change scores across this period were significantly different between the two conditions with the control condition having a larger increase in LAN than the artwork condition.

Table 10

Differences Between Control and Artwork Conditions in Mean Change Scores of the AVI Component Scores from Post-Stressor to Post-Viewing Period, Controlling for Post-Stressor Scores

AVI component	Control, adj M(SD)	Artwork, adj M(SD)	*F*	*df*	*p*	η_p^2
High arousal positive	-2.19(2.36)	-1.68(1.39)	0.62	1, 27	.440	.02
Low arousal positive	2.13(4.18)	2.41(4.22)	0.04	1, 27	.840	.00
Positive	0.05(2.41)	1.02(1.44)	2.09	1, 27	.160	.07
High arousal negative	-1.16(1.62)	-0.71(1.18)	0.80	1, 27	.380	.03
Negative	-0.12(0.83)	-0.08(0.70)	0.02	1, 27	.879	.02
Low arousal negative	3.67(3.11)	1.46(2.42)	4.55	1, 27	.042*	.14
Low arousal	2.23(2.26)	1.23(2.23)	1.61	1, 27	.215	.06
High arousal	-1.19(2.31)	-0.48(1.30)	2.92	1, 27	.099	.10

Note: positive change scores indicate an increase in the parameter, while negative change scores indicate a decrease. Adj *M*=adjusted mean change score (post-viewing period – post-stressor), controlling for post-stressor scores, *SD*= standard deviation, *p<.05

6.4.2 Fatigue and Drowsiness

Kruskal Wallis Tests were conducted to examine the effect of condition on fatigue and drowsiness after the viewing period. There was a significant difference in drowsiness between the conditions ($H_{(1)}$= 4.30, p=.038, η_p^2=.12), with the scrambled condition indicating more drowsiness (*mean rank*= 18.40) than the landscape condition (*mean rank*=12.60). The difference in fatigue between conditions after the viewing period approached significance ($H_{(1)}$= 3.64, p=.057, η_p^2=.09) with the scrambled condition reporting more fatigue (*mean rank*=18.23) than the landscape condition (*mean rank*=12.77).

6.4.3 Salivary Stress Biomarkers

No significant main effects were observed for the effect of condition on sCort ($F_{(1,26)}$=1.11, p=.302, η_p^2=.17) or sAA ($F_{(1,26)}$=1.53, p=.227, η_p^2=.22). A significant main effect of time was found for sCort ($F_{(3,68)}$=7.87, p<.001, η_p^2=.98). Follow-up polynomial contrasts indicate a significant linear trend ($F_{(1,26)}$=18.03, p<.001, η_p^2=.98), with sCort decreasing over the course of the experiment in both conditions: baseline (M=1.03, SD=0.84), post-speech (M=0.76, SD=0.94), during viewing (M=0.76, SD=1.04) and post-viewing (M=0.59, SD=0.82). There was not a significant main effect of time for sAA ($F_{(2,58)}$=0.89, p=.427, η_p^2=.21).

There were no significant interaction effects of time-point and condition on sCort ($F_{(3, 68)}$=1.72, p=.176, η_p^2=.40) or sAA ($F_{(2, 58)}$=1.65, p=.197, η_p^2=.36). However, there was a significant difference between conditions in the quadratic trends in sCort over the session ($F_{(1,26)}$=4.49, p=.044, η_p^2=.53). Follow-up contrast analysis showed the quadratic trend was significantly greater for the landscape condition (M=0.37, SD=0.78) than the scrambled condition (M=-0.19, SD=0.61), indicating that the landscape condition had a significant inverted U-shape relationship where cortisol levels decreased from baseline, but increased again after the viewing period. The scrambled condition did not have this U-shaped relationship.

ANCOVAs for change scores across the viewing period (after the stressor until after the viewing period) controlling for baseline levels were conducted for sCort and sAA. Change scores for sCort over the viewing period showed a significant difference between conditions when controlling for baseline sCort ($F_{(1,26)}$=5.49, p=.027, η_p^2=.62). The scrambled condition had a significantly greater mean decrease in sCort over the viewing period (M=-0.36, SD=0.43) than the landscape condition, which stayed fairly stable (M=0.02, SD=0.37). This demonstrates that during the viewing period, the scrambled condition had a larger decrease in

sCort levels. Change scores over the viewing period showed no significant differences in sAA between conditions when controlling for baseline values ($F_{(1,26)}$=0.22, p=.216, η_p^2=.23).

6.4.4 Changes in Pupil Size

Pupil size data was not available for one participant, in the landscape condition, due to technical difficulties. Results for the remaining participants are shown in Figure 12, which illustrates moment-to-moment changes in pupil size during the 60 second viewing period. Each plot shows the difference between pupil size at each viewing time-point, averaged across image trials, and mean pupil size, averaged across trials, during the four seconds of viewing a uniform grey screen, prior to each image. Data are shown separately for each block of viewing trials. As Figure 12 shows, in both blocks of trials, and for both conditions, image presentation was associated with a phasic pupil constriction within the first one to two seconds, followed by an extended period in which pupil size remained relatively constant. From very early in the trial (including during the phasic response to image onset) until the end of the viewing period, mean pupil area was larger for the landscape condition, relative to the scrambled condition. Following the initial phasic response to image onset, the pupils of the landscape condition remained larger than when viewing the uniform grey screen. In contrast, the pupil area of the scrambled condition remained similar to the mean pupil size recorded during the pre-image grey screen.

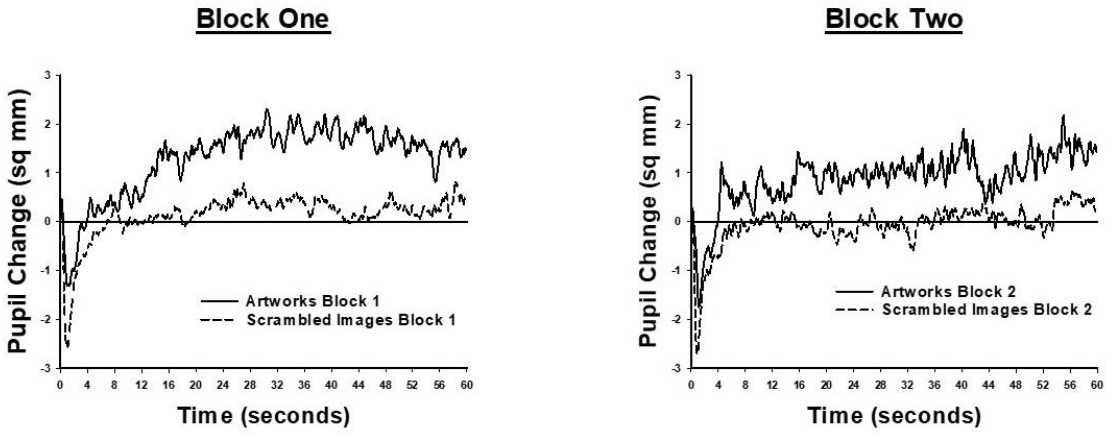


Figure 12. Moment to moment changes in pupil size, when participants viewed landscape artworks (solid lines) and scrambled images (dashed lines). Each plot shows the difference between pupil size at each time-point during the 60-second image viewing period and average pupil size when viewing the uniform grey screen presented before each image. The left-hand panel shows data from the first trial block, comprising 17 images; the right-hand panel shows data from the second trial block, comprising nine images.

Statistical analyses confirmed this description of the pupil size findings. The main effect of trial block was significant ($F_{(1,27)}$=35.43, p<.001, η_p^2=.57) showing that mean pupil size was significantly larger in block two (M=24.69, SE=.51) than block one (M=23.10, SE=.48). The main effect of image was significant ($F_{(1,27)}$=5.40, p=.028, η_p^2=.17), however, this effect was qualified by an interaction with condition ($F_{(1,27)}$=4.74, p=.038, η_p^2=.15). This interaction was analyzed further by assessing effects of image separately for each condition. For participants in the landscape condition, pupil size was significantly larger when viewing a landscape artwork (M=24.99, SE=.93) than when viewing a grey screen (M=23.90, SE=.75, $F_{(1,13)}$=6.41, p=.025, η_p^2=.33). For participants in the scrambled condition, pupil size when viewing a scrambled image (M=23.36, SE=.56) and a grey screen (M=23.32, SE=.51) did not significantly differ (F<1, η_p^2=.002). These results demonstrate that viewing landscapes led to an increase in pupil size which was not seen in the scrambled condition.

6.5 Discussion

The aim of this research was to investigate whether viewing nature artwork in the form of landscape paintings could improve psychological and physiological responses after a stressor, compared to viewing scrambled versions of the artwork that blurred perceptual details. This pilot study was conducted to assess feasibility and estimated effect sizes and was not powered to detect significant effects. Nonetheless, there were some significant effects, and these results will inform a larger study.

Viewing the scrambled images compared to the landscape images led to an increase in low arousal negative affect (feeling dull, sleepy and sluggish) and drowsiness. These subjective ratings are consistent with observations of pupil size. While viewing scrambled images, average pupil size was similar to when participants viewed a uniform grey screen, and smaller than when viewing landscapes. Physiological work has shown a remarkably close relationship between moment-to-moment changes in pupil size and activity in the locus coeruleus of the brain stem (Aston-Jones & Cohen, 2005; Joshi et al., 2016). The locus coeruleus plays a key role in the regulation of arousal. Accordingly, our observation of reduced pupil size is consistent with subjective reports that while participants viewed the scrambled images, they experienced feelings of drowsiness and low arousal.

This is the first study to examine the effects of scrambled images or artworks on cortisol. Contrary to our hypothesis, sCort levels decreased faster after viewing the scrambled images compared to the landscape artworks. Cortisol has been linked with higher alertness and lower fatigue (Tops et al., 2006), so these results suggest that people in the scrambled condition felt less stimulated. Again, these results are consistent with the pupil size findings, as increased pupil size has been associated with increased cognitive engagement, effort and increased arousal (Laeng et al., 2012; Sirois & Brisson, 2014). Taken together, these results suggest

that the landscapes were more stimulating and engaged the viewers more than the scrambled images. This may be because artwork can be a form of visual environmental enrichment.

These preliminary results support theories and research on nature and demonstrate that these effects may translate to nature represented through art. The finding that landscape paintings led to less drowsiness, larger pupil size and higher cortisol supports Kaplan's (1995) ART theory which proposes that nature engages attention and therefore reduces the fatigue effects caused by stress. These results also agree with research which has found that viewing nature leads to 'wakeful relaxation' compared to viewing urban scenes (Ulrich, 1981).

These results also support Wang and colleagues (2015) who suggest that traditional Chinese paintings, where perceptual details are blurred, increased an 'inward oriented' frame of mind inducing high levels of relaxation and mind wandering. This was in contrast to viewing realistic paintings that had the opposite effect and was occupied with a high level of attention and stimulation. Blurred images, which are plentiful in abstract art, traditional Chinese painting and Impressionism, could be examined in a larger study, with the aim of informing an effective and integrated multi-sensory approach to recovery. Therefore, the scrambled images may have acted similarly to abstract art and traditional Chinese paintings.

However, the findings that the landscape artworks increased stimulation also contradict previous research which demonstrated that viewing nature murals compared to no mural led to lower arousal as indicated by decreased HR (Heerwagen, 1990). However, this previous study was conducted with dental patients awaiting procedures, and therefore the nature mural may have worked more as a distraction, rather than being restorative.

This study had a number of limitations. Most importantly, as a pilot study, this study had a small sample size which limited the power of the analyses to find significant effects. Future

research should expand on this study with a larger and more diverse sample, including a larger diversity of ages and cultures. Secondly, the study was conducted in a laboratory setting which may have affected the ecological validity, making it difficult to generalise the results to everyday settings where artwork may be placed to improve health, such as in hospitals.

A further limitation was that the landscapes contained more realistic and recognisable features than the scrambled images. Therefore, the results may have been due to the realism of the artwork rather than the natural content. Future research should include urban landscapes and their corresponding scrambled images, as well as natural landscapes and their scrambled versions, to see whether realism or nature is the effective component.

Lastly, there was little indication that the TSST lead to a physiological stress response in participants with no increase in stress biomarkers observed. It may be that participants were not given enough time to acclimatise before taking the baseline saliva sample and were therefore feeling anxious at baseline. Also, the samples were taken around 15 minutes after the beginning of the stressful task. Research demonstrates that a peak in cortisol is expected at least 20 minutes after the onset of acute stress exposure and therefore this study may not have allowed enough time to sample the entirety of the physiological stress response (Dickerson & Kemeny, 2004; Kirschbaum & Hellhammer, 2007). Future research should allow for a longer sampling time after the stressor and the artwork viewing of at least 20-30 minutes to potentially ensure more reliable stress biomarker findings.

Research on the effects of viewing artworks on stress responses could consider multiple factors. These include content, perspective, colour, composition and level of abstraction. Research also needs to consider whether the art is viewed before or after a stressor. It would be difficult for one study to include all of these factors. This study compared landscape

artworks with mostly natural content with a moderate level of realism to scrambled images after a stressor, and found that the landscapes were more stimulating than the scrambled images. More research is needed to consider the role of other factors, such as those listed above.

6.6 Conclusion

This pilot study gives an early indication that landscape artworks may reduce drowsiness and increase stimulation after stress compared to their scrambled images. We have yet to research whether the same results would be found for other types of artworks. This study sets up a framework to further explore these effects in a larger and more diverse sample. It is recommended that future research allow for a longer sampling time after the experimental tasks to be able to detect possible differences in salivary stress hormones, conduct the research in a more naturalistic setting and use multiple control images. If certain kinds of artworks are found to be beneficial, this could inform their use in stressed population.

Chapter 7- Evidence for the effects of Viewing Visual Artworks on Stress Outcomes: A Scoping Review

7.1 Preface

The results from Study 4 were in contrast to the hypothesises. Instead of decreasing stress and increasing relaxation as expected, viewing the landscape artworks actually increased stimulation. The hypotheses from this study were informed by research on the effects of nature on stress and extrapolated to nature artworks. However, it may be the case that viewing artworks themselves have different effects on stress outcomes. Therefore, it is pertinent to evaluate the evidence for the effects of viewing artworks on stress.

Similar to the nature theories described in Chapter 6, the literature suggests that artworks are a form of positive distraction. In this way, artworks effortlessly capture attention and cause viewers to be 'transported' to another place (George et al., 2017; Karnik et al., 2014). This ultimately diverts attention away from negative experiences and emotions, such as stress and pain (Evans et al., 2009; Hathorn & Nanda, 2008). Artworks can also elicit positive emotions and cognitions, which can replace negative feelings and thoughts (Vartanian & Skov, 2014). Therefore, theoretically viewing artworks should be able to decrease stress levels.

Although widely used in clinical practice, and anecdotally accepted as fact, there is little high-quality evidence for the effects of viewing artworks on stress and health outcomes. Most research instead focusses on the effects of active participation in making artworks, rather than passively viewing them. Preliminary research supports the idea that viewing artworks can reduce stress; however, much of this research is low-quality, anecdotal or descriptive, with very few high-quality randomized trials conducted on this topic. Due to the limited evidence

base, it is important to review the existing evidence to be able to direct focus for future research.

Therefore, a scoping review was conducted for the final manuscript of this thesis which aimed to evaluate the existing evidence on this topic and identify any research gaps. Existing systematic reviews have been conducted on the effects of nature elements (Jo et al., 2019), visual arts-based interventions (Carswell et al., 2018), and interior design, including artworks, (Daykin et al., 2008; Vetter et al., 2015) on stress and health outcomes. However, at the time of writing, no reviews have been conducted on the effects of passively viewing artworks on stress.

Due to the large heterogeneity in methodology and outcomes, and low quality of the existing research, a scoping review was conducted instead of a full systematic review and quality assessment. The review directs future research to fill in evidential gaps to eventually facilitate the creation of a full systematic review and meta-analysis. Of particular note, the review highlighted possible moderating factors in the relationship between viewing artworks and stress. These moderating factors (including context, individual characteristics, artwork content and choice) may influence whether artwork is physiologically relaxing or stimulating to viewers. If artworks reduce stress through distraction, then artworks are likely to be more effective during the stressful period itself, rather than during the recovery period. This may explain the unexpected effects seen in Study 4 and highlights important considerations for future research.

7.1.1 Citation

Law, M., Karulkar, N., & Broadbent, E. (in submission). Evidence for the effects of viewing visual artworks on stress outcomes: A scoping review.

7.2 Introduction

A number of studies suggest that participation in the arts is beneficial for health. This has resulted in a proliferation of different arts programmes. Many healthcare and workplace settings offer art programmes to reduce stress and improve wellbeing for staff, patients and customers (Hathorn & Nanda, 2008). However, there is little evidence that these programmes have the desired effects and there is a need for a high-quality evidence base for art-based interventions (Boyce et al., 2018; Vetter et al., 2015).

Engagement with arts can be divided into active and passive participation. Active participation involves making, creating or teaching arts; whereas passive participation involves behaviours such as observing, viewing, listening and watching art (Carswell et al., 2018; Davies et al., 2012). Passive viewing of artworks is an easy, low-cost and non-invasive intervention; however, research is lacking compared to the substantial evidence base for the active participation in artwork making and art therapy. This scoping review focussed on the effects of passively viewing visual artworks and therefore excluded research pertaining to the active participation in arts.

There is some evidence that viewing artworks is beneficial; however, this evidence is not of uniformly high quality, is rarely critical, and is sparse, with many important theoretical and evidential gaps. As well as this, most of the evidence comes from anecdotes, descriptions and personal experiences, rather than empirical research (Lankston et al., 2010; McCabe et al., 2013). Although many settings have been used within this research, including healthcare, art museums and laboratories, there is a paucity of evidence to demonstrate whether these settings affect outcomes differently. Demographics may be important moderators as ethnicity, gender and age may influence preferences for certain types of artworks. However, rigorous research has yet to be conducted examining the influence of settings and populations.

Due to these limitations, it is important to review the existing evidence and identify any research gaps that need to be addressed. As the evidence base is small and heterogeneous, a systematic review cannot be accurately completed, so instead a scoping review was conducted. The results can be used to direct future research to fill these gaps before a full systematic review can be completed.

There is no universally accepted definition of artworks as this construct has been inconsistent and debated. For the purpose of this review, artwork was defined as two-dimensional artistic works made primarily for their aesthetics, rather than any functional purpose. This definition was created from working definitions of visual and fine arts used in previous research (Eisen et al., 2008; Lacey et al., 2011). Based on this definition, this review included studies on paintings, drawings and prints and excluded studies on sculpture, films, interior design or architecture. Photographs were only included if they depicted artworks. Digital artworks were included.

Viewing artworks is a form of visual environmental enrichment and is theorised to be stress-reducing through positive distraction (George et al., 2017; Lankston et al., 2010). To explore this theory, the review focused on the effects of viewing visual artworks on stress outcomes. Both psychological and physiological stress outcomes were included.

7.2.1 Objective and Research Questions

The aim of this scoping review was to systematically examine the extent of existing research available on the effects of viewing visual artworks on stress outcome measures and identify knowledge gaps to aid future research. The following research question was formulated: what research has been conducted on the effects of viewing visual artworks on stress outcomes in any populations and settings?

Several secondary questions were developed:

- What populations and settings were studied?
- What stress outcomes were measured?
- What type and content of artworks were viewed?
- What was the duration of the artwork viewing and how many artworks were viewed?
- Were the interventions effective in changing the outcomes?
- What is the methodological quality of the existing studies?

A preliminary search for previous reviews on this topic was conducted on Google Scholar, JBI Evidence Synthesis and the Cochrane Database of Systematic Reviews prior to creating the protocol.

7.3 Methods

7.3.1 Protocol

A scoping review protocol was developed based on the Joanna Briggs Institute methodology for scoping reviews (Peters et al., 2020) and using the preferred reporting items for systematic reviews and meta-analyses extension for scoping reviews (PRISMA-ScR). The objectives, eligibility criteria and methods were specified in advance and documented in the protocol registered at osf.io/gq5d8.

7.3.2 Eligibility Criteria

Studies had to meet the following inclusion criteria; be a primary study where participants passively viewed at least one visual artwork as an intervention, including viewing paintings, drawings, prints, digital artwork, or photographs of artworks, and measured at least one stress outcome measure (physiological or psychological indices). Measures of anxiety or mood were not considered as direct measures of stress and therefore fell out of the scope of this

review. Unpublished research, including working papers, theses/dissertations and conference proceedings were included.

Studies were excluded if participants had active engagement in the arts (e.g. studies on art therapy or the production/creation of art), the study investigated the effects of interior design, architecture, sculpture, films or photography not depicting artworks, and review papers, including systematic reviews, scoping reviews and meta-analyses.

Due to the small and heterogeneous nature of this research area, there were no restrictions in terms of populations, contexts, dates of publication or study designs. However, during the screening phase, it was decided to exclude qualitative studies as these studies did not have clear stress outcomes, which was a key inclusion criterion. Only English studies were considered.

7.3.3 Search Strategy

To identify potentially relevant studies, the following electronic databases were systematically searched; Medline, Embase, APA PsycINFO, Cochrane CENTRAL, Scopus and Google Scholar (first 30 pages), with the help of a subject librarian. The search string combined a set of artwork and stress terms within each set with “OR” and between the two sets with “AND.” The search was first conducted using an extended list of search terms from the registered protocol; however, this search strategy resulted in a large number of irrelevant articles. Therefore, in the final search, some of the more ambiguous search terms were removed to refine the search further. For example, the term 'drawing' was removed as this could refer both to artistic drawings and ‘drawing’ blood. The final search strategies for two example databases are presented in Table 11.

Table 11

Example Search Strategy Syntax for Databases

Database	Search Strategy Syntax
Scopus	(TITLE-ABS-KEY (artwork OR "art work" OR "visual art" OR "art museum" OR painting OR mural OR "works of art" OR "viewing art" OR "viewing artwork" OR "artwork viewing" OR "art gallery" OR "art galleries") AND TITLE-ABS-KEY (stress OR "blood pressure" OR anxiety OR "heart rate" OR mood OR norepinephrine OR epinephrine OR "stress hormones" OR stressor OR glucocorticoids OR cortisol OR alpha-amylase OR "stress reduction")) AND (LIMIT TO (LANGUAGE , "English"))
ProQuest Dissertations and Thesis	ab(artwork OR “art work” OR “visual art” OR “art museum” OR painting OR mural OR “works of art” OR museum OR “viewing art” OR “artistic work” OR “viewing artwork” OR “artwork viewing” OR “art gallery” OR “art galleries”) AND ab(stress OR “blood pressure” OR anxiety OR respiration OR “heart rate” OR mood OR norepinephrine OR epinephrine OR “stress hormones” OR “mental health” OR stressor OR glucocorticoids OR cortisol OR alpha-amylase OR “immune marker” OR “stress reduction”)

The grey literature was searched using the same search terms to identify any unpublished studies. Grey literature databases searched included; Google (limited to the first 20 pages), ProQuest theses and dissertations database, APA PsycExtra and Opengrey.eu.

A search was then conducted by hand of the reference lists of relevant identified articles. Lastly, the ‘cited by’ feature of Google Scholar was used to see if any of the relevant studies had been cited by undetected articles. All extracted references from these searches were imported to RefWorks and all duplicates removed. The final search was executed on 27 May 2020. The number of studies identified by the search strategy is shown in Figure 13.

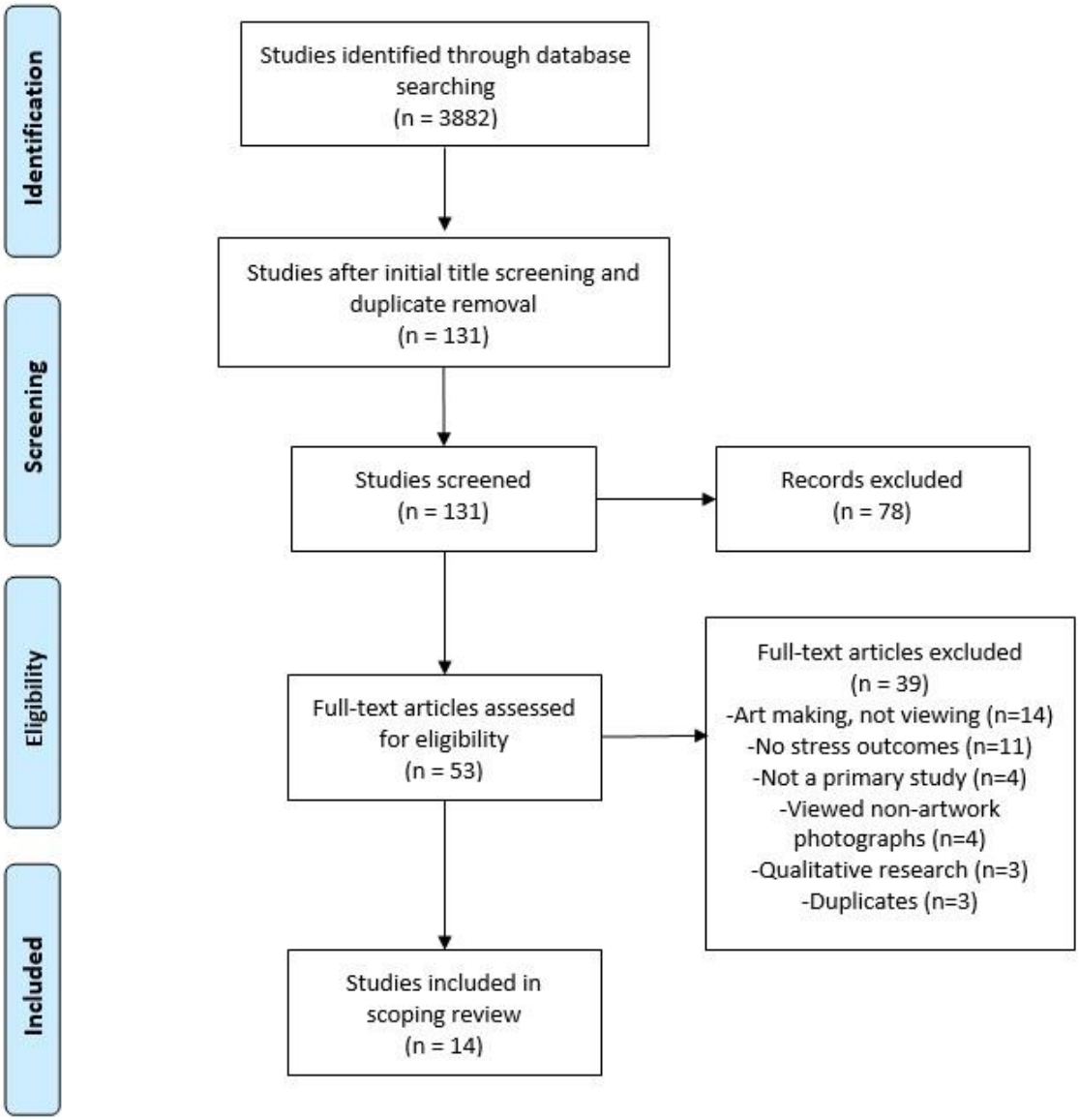


Figure 13. PRSIMA-ScR flow diagram of the study selection process.

7.3.4 Screening and Study Selection

Screening of the studies identified by the search strategy was conducted by two independent reviewers using a two-staged approach using the programme Covidence. Due to the high volume and large amount of unrelated studies identified, one author initially screened the titles and removed any irrelevant studies, before the first stage. In the first stage of screening, two reviewers independently screened the abstracts for the eligibility criteria. If

a study's eligibility was judged to be uncertain, the article was included in the second stage. In the second stage, two reviewers screened the full texts of the studies to determine final inclusion or exclusion based on the eligibility criteria. The two stages were conducted by the reviewers independently, with the results of each stage discussed. Any disagreements related to eligibility of an article were discussed and agreement was reached. The number of included and excluded studies at each stage of the screening procedure is shown in Figure 13, with reasons for exclusion.

7.3.5 Data Extraction and Analysis

Data was extracted from each included study into a charting form by the two reviewers independently. This charting form was developed in accordance with the review questions. It included; publication details (i.e. title, year, authors), methodology (i.e. aims, design, population characteristics, setting, outcomes), artwork details (i.e. type and content of artwork, duration of artwork viewing, number of artworks), key findings related to scoping review questions, and items to assess methodological quality (i.e. registration details, comparator groups, randomisation, blinding, power analyses).

The charting form was iteratively refined during the extraction process to ensure all useful information was extracted. The charting form was first independently pilot tested by the two reviewers on a random sample of four studies. The reviewers discussed this process and amended the charting form by adding a column about the artwork viewing directives given to the participants. Data extraction was then completed for the remaining studies independently by the two reviewers and any inconsistencies were discussed. This extracted data is reported in tabular and descriptive text format to answer the review questions.

7.4 Results

As shown in Figure 13, the search strategy resulted in 3882 texts, which were screened for eligibility. After the initial title and abstract screening, the full text was retrieved for 53 articles and examined against the eligibility criteria. During this process, three theses were found to have matching published journal articles and therefore were excluded as duplicates. The remaining excluded articles did not meet the eligibility criteria. This screening narrowed the studies down to 14 articles for inclusion.

The design and key findings related to the stress outcomes of each study are briefly detailed in Table 12, with specific details regarding the secondary review questions provided in Table 13. All 14 articles were primary studies published as journal articles. Apart from the duplicate theses mentioned above, no grey literature met the eligibility criteria for inclusion. The studies' publication dates ranged from 1972 to 2020. Eight studies came from Europe, four from the United States of America and one each from Australia and New Zealand.

Table 12

Summaries of the Studies' Designs and Key Stress Outcome Findings

Study	Study Design and Key Findings
Clow & Fredhoi (2006)	Studied self-reported stress and arousal, and sCort levels in a group of London city workers during a lunchtime visit to an art gallery. Measurements were taken before and after the 35-40-minute gallery visit to explore pre-post intervention changes. Self-reported stress and sCort levels both decreased over the intervention. There were no differences in arousal levels.
D'Cunha et al (2019)	Evaluated the psychophysiological effects of attending the National Art Gallery of Australia Art and Dementia programme. People living with dementia attended the group-based, six-week programme which involved viewing and discussing artworks, led by an art director. Measures of sCort and IL-6 were taken at baseline, at the end of the programme and 12 weeks later. Waking sCort levels increased from baseline to post-intervention, but decreased at follow-up. No changes in evening sCort or IL-6 were observed. The ratio of waking to evening sCort increased from baseline to post-intervention indicating a more dynamic diurnal cortisol rhythm.
de Jong (1972)	Three groups of participants (advanced art history students, advanced fine art students and laboratory workers as controls) viewed projections of 12 paintings considered to be 'beautiful' and 12 paintings considered to be 'ugly' in a random order while their HR, respiration rate and skin conductance was measured continuously. The fine arts and art history students showed a greater change in skin conductance than the laboratory workers. Respiration and skin conductance were higher during the 'beautiful' paintings than the 'ugly' paintings in all groups. The fine arts students had faster HR during the 'beautiful' paintings compared to the 'ugly' paintings, however, for the other two groups, this result was reversed.
Eisen et al (2008)	The third phase this study investigated which type of art was most effective in reducing stress in paediatric patients. On arrival to the hospital, patients were randomly allocated to one of three rooms; a room with a nature artwork, a room with an abstract artwork or a room with no artwork. Self-reported stress, BP and respiratory rate were taken at baseline and after two hours of exposure to the artworks. Overall, there were no significant differences between the groups on stress, BP or respiration. However, sub-analyses showed that significantly more males than females in the 8-10 age group were positively affected by the nature artwork, as demonstrated by decreased self-reported stress, BP and respiratory rates.
Karnik et al (2014)	Installed a diverse collection of artworks in the public spaces and clinic rooms of a hospital. Patients were retrospectively contacted with a survey which included evaluating whether the art installations changed their self-reported stress levels. 61% of the patients that reported seeing the artworks stated that the artworks somewhat or significantly reduced their stress levels.
Krauss et al (2019)	Participants viewed six Flemish expressionism artworks in an art museum, while HR and skin conductance were continuously measured. Participants

	were randomly assigned to either receive descriptive information about the artworks (described the artwork in a declarative way) or elaborative information about the artworks (described the context and deeper meaning behind the artworks). There were no significant differences in HR, HRV or skin conductance between the two groups. However, in both groups HR was lower, and skin conductance and HRV higher when viewing the artworks, compared to baseline.
Kweon et al (2008)	Conducted an experiment investigating the effects of artwork posters on stress and anger levels in an office setting. Students were asked to complete a series of stress and anger provoking computer tasks in one of four different mock office conditions; an office with nature posters, abstract posters, both nature and abstract posters or no posters. Levels of self-reported stress were measured across the experiment. Males had the highest stress levels in the office with no posters, and the lowest stress levels in the office with mixed art posters. On the other hand, females had the highest stress in the office with all abstract posters and the lowest levels in the office with all nature posters. However, these results were only significant for males and not females.
Law, Minissale et al (2020)	Conducted a pilot study to investigate whether nature artworks could improve recovery from a laboratory stressor. Participants were randomised to either view a 30-minute digital slideshow of landscape artworks or digitally scrambled versions of these artworks after being exposed to a laboratory stressor. Saliva samples were taken at baseline, after the stressor, during the art viewing and after the art viewing to measure cortisol and alpha-amylase. sCort levels decreased more rapidly while viewing the scrambled images compared to the landscape artworks. There were no changes in sAA across the experiment or between groups.
Mastandrea et al (2019)	Students visited an art museum and were randomly assigned to visit one of three art exhibitions for five minutes; a figurative art exhibition, a modern art exhibition or a museum office as a control condition. BP and HR were measured before and after the visit. Systolic BP decreased in all groups; however, this decrease was only significant in the figurative art group. HR also decreased in all three groups, however, there was no significant differences between groups.
McCabe et al (2013)	Evaluated the effects of the Open Window art intervention on stem-cell transplantation patients. The Open Window is a virtual window which is installed in a hospital room, where the patients can switch through nine art channels with different artworks. Patients were randomised to either a room with the Open Window or not. Self-reported distress was measured at admission, the day before transplant, seven days after transplant, prior to discharge, and 60 days, 100 days and six months post-transplant. Results demonstrated no significant differences in levels of distress between the two groups at any of the time-points.
Pearson et al (2019)	Examined the impact of nature-themed window murals on physiological measures in paediatric patients. Paediatric patients were assigned to hospital rooms with either a fish-themed window mural, a tree-themed window mural or no window mural. Patients' BP and HR were taken retrospectively from the patients' medical records. Those patients with the window murals had significant improvements in HR and systolic BP, with the tree-themed mural having the greatest effect.

Siri et al (2018)	Examined the effects of viewing original physical artworks and their digital reproductions within a museum context. Cardiovascular variables were measured via ECG continuously in healthy volunteers while viewing two real abstract paintings and their digital reproductions. Results showed that there was a significant difference in HR between viewing the two real paintings, but no difference was found between the digital reproductions, or between the real and digital reproductions. No differences in HRV were found.
Tschacher et al (2012)	Monitored the physiology of visitors to an art museum using an electronic sensor glove which recorded physiological data and locomotion activity while they viewed the artworks. Afterwards, they were asked to rate the aesthetic qualities of some of the artworks. HRV increased while viewing artworks that were deemed beautiful, high quality and surprising/humorous. Skin conductance variability increased, and HR decreased while viewing more dominant artworks (artworks experienced as dominant and stimulating by the viewers).
Wikström et al (1993)	Investigated whether visual stimulation could improve the health of elderly women living alone. The women were randomised to either an intervention or control group. The intervention group were shown a selection of pictures, including artworks, and asked to discuss them, whereas the control group discussed current events. BP was measured at baseline, immediately after the intervention and four months later. The intervention group had significantly lower systolic BP than the control group after the intervention and at follow-up

Table 13

Overview of Studies Included in the Review

Study	Study Design	Comparator Group	Setting	Population (N)	Stress Outcome Measures	Type and Content of Artwork	Quantity of Artworks Viewed by Each Participant	Duration of Artwork Viewing
Clow & Fredhoi (2006)	Pre- and post-test, within groups quasi-experimental study	None	Art gallery	Office workers N=28 (25 included in the analysis)	Self-reported stress Self-reported arousal sCort	Physical artworks in a gallery- exact content not specified	Not specified- gallery exhibition	35-40 minutes in the gallery
D'Cunha et al (2019)	Pre- and post-test, within groups quasi-experimental study	None	Art gallery	People living with dementia N=28 (22 included in the analysis)	sCort IL-6	Physical artworks in a gallery- exact content not specified	3-4 artworks each session, over 5-6 sessions	5-6x 90-minute sessions. Each artwork was viewed for 20 minutes
de Jong (1972)	Between groups experimental study	Laboratory workers (non-art students)	Laboratory	Advanced art history students, advanced fine arts students and laboratory workers N= 27	HR Skin conductance Respiration rate	Digital projections of 12 paintings considered 'beautiful' and 12 paintings considered 'ugly'	24	Each painting was viewed for 10 seconds
Eisen et al (2008)	Pre- and post-test, randomised controlled trial	Room with no artwork	Hospital- patients' room	Paediatric patients (aged 5-17) N=78	Self-reported stress HR BP Respiratory rate	One group had a representational nature artwork hung on the wall, whereas the other group had an abstract artwork hung on the wall	1	2 hours
Karnik et al (2014)	Cross-sectional survey	None	Hospital- public spaces and clinic rooms	Hospital patients N= 826	Self-reported change in stress	Physical collection of abstract and representational imagery (including nature imagery). Includes an assortment of artistic	Collection of over 5300 artworks	N/A

						media; and a variety of subject matter		
Krauss et al (2019)	Randomised controlled trial	Group received only descriptive information about the artwork (compared to elaborative information)	Art museum	General public aged between 18 and 35 N= 75	HR HRV Skin conductance	Physical abstract paintings of Flemish expressionism	6	Not specified
Kweon et al (2008)	Between groups experimental study	No artwork posters group	Laboratory (replicated office setting)	Psychology students N=210	Self-reported stress	Nature posters and abstract posters	4	Not specified
Law, Minissale et al (2020)	Between groups experimental pilot study	Scrambled artwork images	Laboratory	General public N=30	sCort sAA	Digital slideshow of either landscape paintings or digitally scrambled versions of these paintings	26	30 minutes
Mastandrea et al (2019)	Between groups experimental study	Museum office	Art museum	Undergraduate students N=77	BP HR	Physical artworks in a gallery- including figurative artworks (e.g. landscapes and portraits) and modern artworks (e.g. abstract, impressionist and informal paintings)	Not specified- gallery exhibition	5 minutes
McCabe et al (2013)	Randomised prospective clinical trial	Room without the 'Open Window'	Hospital- patients' room	Stem cell transplantation patients N= 199 (164 included in the analysis)	Self-reported distress	Virtual window, with artwork projections. Artwork collections ranged from visually complex abstract images to images of nature.	Not specified- 9 art 'channels,' each with a collection of artworks	For the duration of their hospital stay- times not specified

Pearson et al (2019)	Pre- and post-test, between groups quasi-experimental study	Room without a window mural	Hospital-patients' room	Paediatric patients aged 2-18) N=90	HR Systolic BP	Window mural- either aquatic or forest themed	1	Minimum of 48 hours
Siri et al (2018)	Within groups experimental study	None	Art museum	General public N=60	HR HRV	2 real abstract contemporary paintings and their digitally produced replicates	4	144 seconds per artwork
Tschacher et al (2012)	Within groups quasi-experimental study	None	Art museum	Museum visitors N=517 (373 included in the analysis)	Skin conductance HR HRV	Physical modern and contemporary art exhibition	76	No specific timeframe given to participants. On average, they spent 28 minutes at the gallery.
Wikström et al (1993)	Pre- and post-test randomised controlled trial	Group that were not shown artworks	Senior citizen apartment	Women aged over 70 N=40	Systolic BP	Physical pictures- ranging from artworks of nature, flowers and people, abstract patterns, white figures on black backgrounds and photographs.	Not specified how many each participant viewed	Not specified

7.4.1 Summary of Study Methodologies

7.4.1.1 Designs. The 14 studies had very different designs and methodologies (see Table 13). Only nine studies used a between groups design. Another four used a within groups design, where measures were compared pre- to post-viewing the artworks, with no comparator groups. The final study used a cross-sectional design, measuring stress-reduction at one time-point.

Of the nine between groups designs, six used a no artwork control group as a comparator, and one used scrambled versions of the artworks. Although the remaining two studies had comparator groups, the viewing directives given to the groups (Krauss et al., 2019) and the art experience of the participants in each group (de Jong, 1972) were different, rather than the artwork viewed.

7.4.1.2 Settings. Six studies were conducted in an art gallery or museum, three in a laboratory, four in hospital rooms or hospital public spaces, and one in senior citizens' apartments. These settings represent a mix of both naturalistic settings with high ecological validity and laboratory settings with high experimental control.

7.4.1.3 Populations. The majority of studies investigated healthy participants in the form of students *(n*=3), office workers (*n*=1) or the general public (*n*=4). Other research used patient populations known to have high stress levels. Four studies investigated hospitalised patients, with two being paediatric samples. Lastly, D'Cunha et al (2019) investigated people living with dementia and Wikström et al (1993), elderly women.

There is little research on whether population type affects stress reactions. Very few studies compared demographic factors, with the following exceptions. de Jong (1972) found that having different art experience affected outcomes. Three studies found significant

differences between the stress-reducing effects of viewing artwork between males and females (Clow & Fredhoi, 2006; Eisen et al., 2008; Kweon et al., 2008). Lastly, one study compared results across different health conditions, but found similar results between groups (Karnik et al., 2014).

7.4.1.4 Outcomes. Nine studies explored only physiological stress measures, three explored only psychological stress measures and the remaining two explored both. The psychological stress measures included; the Cox Mackay Stress Arousal checklist (Mackay et al., 1978), a stress adjective checklist (King et al., 1983), Likert scales, and a distress thermometer (Roth et al., 1998). The physiological measures were mainly cardiovascular, including BP, HR and skin conductance, which were measured in eight studies. Salivary biomarkers were measured in three studies including sCort, sAA and IL-6. Respiration was measured in two studies.

7.4.2 Summary of the Artwork Interventions

7.4.2.1 Types of artworks. 10 studies used physical artworks. Most were original paintings, however one study used posters depicting artworks (Kweon et al., 2008) and another used a window mural (Pearson et al., 2019). Another three studies used digital reproductions of artworks. Two used slideshows of digital images (de Jong, 1972; Law, Minissale et al., 2020), whereas the third used the Open Window, which digitally projected artworks (McCabe et al., 2013). The last study directly compared physical artworks with their digital reproductions (Siri et al., 2018). This study did not find any differences between the types of artwork, indicating that digital reproductions may be just as stress-reducing as physical artworks.

7.4.2.2 Content of artworks. The content ranged from representational nature images, to complex abstract artworks. Four studies provided an assortment of artwork content in one

exhibition and therefore it could not be determined whether content was influential. Two studies investigated the effects of abstract artwork but did not compare these to another artwork type. Another study (de Jong, 1972) compared the physiological effects of artworks rated to be 'ugly' or 'beautiful.' Although the exact content of the artwork was not described, this study did find that participants had higher skin conductance and respiration rates while viewing the 'beautiful' paintings, compared to the 'ugly' paintings, demonstrating that the aesthetic content of the artwork may influence their effects.

Another four studies investigated the effects of viewing nature artworks. Two studies found that self-reported stress was lower when viewing nature artworks compared to abstract artworks (Eisen et al., 2008; Kweon et al., 2008). One study found that different aspects of nature might have stronger effects; a forest mural resulted in larger BP decreases than an aquatic mural (Pearson et al., 2019). Nature content may also affect biological indicators of stress responses; cortisol levels decreased faster after a stressor in people viewing scrambled versions of nature artworks, compared to the original nature artworks (Law, Minissale et al., 2020).

The remaining two studies did not report on the content of the artwork and therefore, cannot be categorised.

7.4.2.3 Duration of artwork viewing. Nine studies reported the duration participants spent looking at the artwork (see Table 13). This ranged from two minutes to over 48 hours. No study investigated whether changing the duration of exposure to artworks affected stress outcomes.

7.4.2.4 Quantity of artworks. Most of the studies did not specify the exact number of artworks viewed. Of those studies that did specify a number, it ranged from one artwork to over 5300 in one exhibition. Half of the studies had participants view a collection of artworks

as an exhibition or art programme. Only two studies showed each participant one artwork and both were in paediatric hospital rooms (Eisen et al., 2008; Pearson et al., 2019). The other experimental studies ranged from viewing four to 26 artworks in one sitting, with the exact numbers provided in Table 13.

7.4.2.5 Viewing directives. Five studies explicitly mentioned the viewing directives given to participants. Two experimental studies told participants to attentively look at and explore each artwork (de Jong, 1972; Siri et al., 2018), whereas another study asked visitors to explore the art gallery in any way they pleased (Clow & Fredhoi, 2006). The remaining two studies asked participants to discuss and describe each artwork to the group and/or art director during art programmes (D'Cunha et al., 2019; Wikström et al., 1993).

7.4.3 Summary of Key Findings

All but one of the studies that measured self-reported stress found a significant decrease after viewing artwork (Clow & Fredhoi, 2006; Eisen et al., 2008; Karnik et al., 2014; Kweon et al., 2008), with the final study showing no significant changes (McCabe et al., 2013). A consistent decrease in systolic BP was also found across the four studies measuring BP (Eisen et al., 2008; Mastandrea et al., 2019; Pearson et al., 2019; Wikström et al., 1993). Skin conductance and skin conductance variability both increased while viewing artworks (de Jong, 1972; Karnik et al., 2014; Krauss et al., 2019). The results for HR were mostly consistent. Two of the three studies that measured HR found that viewing artworks decreased HR (Pearson et al., 2019; Tschacher et al., 2012). The other study found that viewing beautiful paintings increased HR for students trained in fine arts and decreased HR for other participants (de Jong, 1972).

The cortisol and respiration results were less consistent. An art gallery visit decreased sCort levels (Clow & Fredhoi, 2006); however, a six week art intervention for people living

with dementia increased waking cortisol levels (D'Cunha et al., 2019). Lastly, after a stressor, sCort decreased faster in those viewing scrambled images, compared to those viewing landscapes (Law, Minissale et al., 2020). Viewing beautiful paintings lead to an increase in respiration rates in a healthy sample (de Jong, 1972). Whereas nature artworks in a hospital room decreased respiration rates in children (Eisen et al., 2008). These studies all had different samples, settings and artworks which may have accounted for these mixed findings. Lastly both sAA (Law, Minissale et al., 2020) and IL-6 (D'Cunha et al., 2019) were each only measured in one study and showed no significant changes.

7.4.4 Summary of Methodological Quality

Many of the studies lacked sufficient methodological details to conduct a full quality analysis and the quality problems have been briefly detailed below. None of the studies were pre-registered. Sample sizes ranged from 27 to 826 participants; however, only two studies conducted a power analysis to determine their sample size. Therefore, it is difficult to determine if all studies were adequately powered.

Only nine studies had comparator groups, with only seven related to the artwork intervention. For most studies, it was difficult to blind the participants, because in most cases participants were explicitly asked to view artworks. However, two studies did successfully blind the study as both the researchers/nurses collecting the measures and the participants were not explicitly made aware of the presence (or absence) of the artworks (Kweon et al., 2008; Pearson et al., 2019). All nine between-groups studies reported randomisation of participants to groups. However, the method of randomisation was not stated in many studies. Only four studies (Eisen et al., 2008; Krauss et al., 2019; McCabe et al., 2013; Wikström et al., 1993) were randomised controlled trials, which are the gold-standard of research.

7.5 Discussion

This scoping review aimed to examine the existing research on the effects of viewing visual artworks on stress outcomes and identify gaps in the research. The 14 included studies demonstrate research in this area is growing, with 10 studies being published in the last 10 years. However, there is still a paucity of studies, and the evidence that does exist has heterogeneous methodologies, creating difficulty in comparing results.

Overall, the evidence supports the claim that viewing artworks can reduce stress, in particular self-reported stress and systolic BP. These preliminary quantitative results support qualitative research showing that viewing artworks provides positive distraction from a hospital environment and lowers self-reported stress (George et al., 2017; McCabe et al., 2013; Suter & Baylin, 2007). However, mixed findings combined with a lack of homologous methodologies means that this claim cannot be concluded without more rigorous research. Future research needs to ensure better methodological quality including: adequate comparator groups, power analyses to ensure sufficient sample sizes, clearly defined randomisation procedures and pre-registration.

The differences between the studies suggest important moderating factors, one of which is setting. The museum context may add to the effects of viewing artwork, as museum related factors may lead to greater appreciation of artwork (Mastandrea, 2019). In addition, viewing artwork in a museum usually involves walking, which has its own stress-reducing effects (Kelly et al., 2018). Laboratory studies remove some of these contextual factors and may provide more specific evidence for the effects of viewing artworks, but they have lower ecological validity. The hospital room is an important setting as patients are often confined to their room for long time-periods and rooms are often deprived of environmental enrichment. Artwork could act as visual stimulation to positively distract patients from their stress, pain and medical conditions. Artwork could also have stress-reducing benefits in other settings

such as waiting rooms and workplaces, which are often related to high stress. More research in these settings should be conducted.

Other possible moderating factors include individual characteristics, although little research has investigated these. Gender differences were found in two of the included studies, with a trend towards females experiencing greater stress-reduction in response to nature artworks (Eisen et al., 2008; Kweon et al., 2008). One small survey found that African Americans and Caucasians have similar preferences for nature artworks (Hathorn & Ulrich, 2001); however, no study has investigated whether culture affects the stress-reducing effects of artworks. Given the diversity in cultures, demographics and individual preferences for artwork, it may be over simplistic to suggest that all individuals experience artwork the same way (Ho et al., 2015).

The findings indicate that the content and aesthetic qualities of artwork are also important considerations. Although mixed, the studies generally indicated that nature, especially greenery, may be the most stress-reducing. This is consistent with research demonstrating that nature artwork is most preferred by adults (Nanda et al., 2008) and children (Eisen et al., 2008). It is theorised that nature artwork has the greatest stress-reducing effects as evolutionarily humans are predisposed to experience restoration as a response to nature scenes (Ulrich et al., 2003). On the other hand, abstract artworks can be seen as challenging, ambiguous and unclear for viewers, leading to increased stress (Mastandrea, 2019; Ulrich, 1992). Other artwork content could be provocative and emotionally inappropriate for certain situations, eliciting anger and dislike. For example, a study by Ho and colleagues (2015) found that certain provocative artworks elicited feelings of loneliness and hopelessness in viewers, suggesting artwork must be chosen carefully.

The mixed findings suggest that under some conditions, viewing artwork may be physiologically relaxing, whereas under other conditions viewing artwork may be physiologically stimulating. The direction of these effects may not only depend upon the content of the artwork, but also the context and viewers' stress levels. Regardless of the direction of effects on physiology, lower self-reported stress may result.

Although this review focussed on the stress-reducing effects of viewing artwork, it may also be important to investigate the stimulating aspects of artwork. For certain populations, such as people living with dementia, visual stimulation and enrichment through artworks could improve other aspects of health, such as cognitive function (D'Cunha et al., 2019). As discussed above, visual stimulation and enrichment may also be important to provide positive distraction from negative experiences. Three studies showed an increase in physiological stress (D'Cunha et al., 2019; de Jong, 1972; Law, Minissale et al., 2020). This increased stimulation may be related to the content of the artworks ('beautiful' vs 'ugly' paintings (de Jong, 1972), or landscapes vs scrambled images (Law, Minissale et al., 2020)) or the types of populations involved (people living with dementia (D'Cunha et al., 2019) and art students (de Jong, 1972)).

Choice may be another important variable. This is especially pertinent in settings where people have little control. Art Carts have been used in hospitals to allow patients to choose which artworks to view during their stay to give them a sense of control over their environment (Suter & Baylin, 2007). Two studies in this review (McCabe et al., 2013; Wikström et al., 1993) gave participants a choice of artwork, however research is yet to investigate whether the element of choice affects stress outcomes.

Directives given to viewers may influence the way participants view artworks and therefore moderate the artworks' stress-reducing effects. Wikström (2011) previously

discussed the importance of creating an art-dialogue when viewing and discussing artworks in order to improve engagement, understanding and empowerment. Other research (Ho et al., 2015) demonstrated that the descriptions given to viewers about artwork could be influential, and therefore this may be an important element for studies to include. However, few studies reported the directives given. It is important for future research to report what directives were provided and investigate whether this is influential.

Finally, it is difficult to determine the dose-response relationship of artwork viewing. There was little consistency in the number of artworks shown to each participant, and no study investigated whether the quantity of artworks or viewing durations mattered. Therefore, future research could investigate the best artwork viewing duration and number of works.

7.5.1 Limitations

This review is limited by only including English articles. Articles in other languages could have been missed. The review deviated slightly from the original protocol. Due to the large number of irrelevant articles identified using the original search strategy, the search terms were narrowed and the original title screening was only conducted by one reviewer. These deviations were required to make the search and screening more feasible. This review did not include anxiety or mood measures or studies using qualitative methodology. These were considered outside the scope of the review as they are not direct stress outcome measures.

7.5.2 Conclusions

This scoping review summarised research on the effects of viewing visual artworks on stress outcomes. 14 studies met the eligibility criteria, with consistent reductions in self-reported stress, but mixed effects on physiology. Most of the research was low quality, with many methodological details missing, and there was high heterogeneity in research methodologies. Setting, individual characteristics, artwork content, and viewing instructions

may be important moderating factors. More robust research, using standardised methods and randomised controlled trials, is needed before strong conclusions can be made about the effects of viewing visual art on stress outcomes.

Chapter 8- Discussion

8.1 Overview

Although EE has been researched extensively in animals, little research has been conducted to investigate whether these effects translate to human populations. Therefore, this thesis aimed to investigate whether the effects of EE on stress and wound healing seen in animal samples can also be found in humans. Four experimental studies and one scoping review were conducted to address this aim. These studies explored the effects of multiple types of sensory EE interventions including; music, comfort items, a Paro robot and viewing artworks on stress and skin healing outcomes. In this discussion, the key findings from these studies are summarised and integrated into existing literature. Possible clinical implications of these findings are then discussed and lastly, limitations and areas for future research are considered.

8.2 Summary of Key Findings

The first experimental study in this thesis, presented in Chapter 3, aimed to investigate whether three different forms of EE could reduce stress and improve skin healing (Law, Jarrett et al., 2020a). Participants underwent a tape-stripping procedure and then were randomised to interact for 30-minutes with one of three EE interventions (comfort items, music or a Paro robot), or to a control group. This study found that the music condition had higher stimulation levels than the control condition, and the comfort condition had significantly lower relaxation levels than the control condition, after the intervention. However, SBR rates after the tape-stripping wound did not significantly differ between the EE conditions and the control condition. Therefore, this study demonstrated that the EE interventions tested were not beneficial for wound healing compared to a control group.

However, methodological limitations may have accounted for the lack of effects including that the sample was not sufficiently stressed and an active control condition was used.

The second experimental study in Chapter 4, addressed these limitations to re-test the hypotheses (Law, Jarrett et al., 2020b). Study 2 therefore aimed to investigate whether interacting with the Paro robot or listening to music for 30 minutes could improve wound healing from an experimental tape-stripping wound, after a stressor, compared to a non-active control condition. The study found that the Paro condition, but not the music condition, had significantly improved SBR compared to the control condition. Similar to Study 1, this study also found that listening to music increased stimulation levels. Study 2 also explored possible mediators of the effects and found that enjoyment levels during the 30-minute intervention period significantly mediated the relationship between condition and SBR. Therefore, Paro may be an effective form of enrichment to improve SBR in humans after a laboratory stressor and this effect may be due to enjoyment.

Study 3, presented in Chapter 5, followed up these significant results and tested their feasibility in a clinical sample. 25 patients with psoriasis participated in a laboratory stress task, before being randomised to either interact with a Paro robot or sit quietly (control condition) for 30 minutes. The feasibility of the intervention was demonstrated, but the inclusion criteria need to be widened to increase practicality of recruitment in future trials. Moderate effect sizes suggested statistically significant effects on TEWL and Raman outcomes could be possible with a larger sample size. Changes in the psychological and Raman spectroscopy outcomes across the experimental session were found, indicating the feasibility of the procedures for future research with a larger sample size.

The second theme of this thesis explored the use of visual EE, in the form of viewing artworks, for stress-reduction. Study 4, presented in Chapter 6, aimed to investigate whether

viewing landscape artworks, as a form of representational nature, could improve psychological and physiological recovery from a laboratory stressor (Law, Minissale et al., 2020). After the TSST, participants viewed a series of landscape artworks (landscape condition) or digitally scrambled version of these artworks (control condition) for 30 minutes. As well as measures of physiological and psychological stress, participants' pupil size was also tracked while viewing the artworks. After the viewing period, the control condition had increased low negative affect levels and drowsiness. sCort levels decreased more rapidly while viewing the scrambled images compared to the landscape artworks. Lastly, pupil size while viewing the landscape artworks was larger than when viewing a blank screen, an effect not seen in the scrambled condition. This pilot study suggests that viewing landscape artworks was more stimulating and reduced drowsiness after stress when compared to viewing scrambled versions of these images. These results are counter to the hypotheses about EE, which theorised that viewing artworks should decrease stress. However, these results suggest that some EE interventions (specifically, viewing landscape artworks) may be stimulating, rather than relaxing.

To follow up these unexpected findings in Study 4, Chapter 7 presented a scoping review of the existing evidence on the effects of viewing visual artworks on stress outcomes and outlined gaps in the research. 14 studies were identified in the review, with heterogeneous study designs, methodologies and artwork interventions. The results of these studies demonstrated consistent reductions in self-reported stress after viewing artworks, but mixed effects on physiological stress measures. The methodological quality of the studies was poor, with many important methodological details missing. Possible moderators for these effects were identified (including setting, individual characteristics, artwork content, and viewing instructions) with suggestions for future research.

Overall, the findings from the four experimental studies show mixed evidence that short-term EE in humans can reduce stress and improve wound healing. Self-reported stress significantly reduced after the 30-minute intervention periods in all conditions in all studies, including the control conditions. This indicates that even 30 minutes of sitting quietly can be stress-reducing, especially after a stress induction task. However, there were significant effects on levels of stimulation between conditions. Music and landscape artworks both increased stimulation levels compared to the control conditions. In the case of music, this did not translate to improved healing rates, and healing was not assessed in Study 4. Paro was the only EE to improve healing, and the effect was shown to be mediated by enjoyment, rather than stress or stimulation levels. Therefore, the mood enhancing effects of interacting with Paro may be behind the effects on improved SBR, whereas the stimulatory effects of music and viewing artworks to date have not been shown to improve SBR. The results from the scoping review suggest that artwork can in fact improve some physiological stress outcomes under some conditions, and that there are important moderating variables to consider. To further understand the effects of EE in humans, it will be important to study these moderators as well as the psychological and physiological mechanisms that underlie different forms of EE.

8.3 Integration into the Broader Literature

8.3.1 Integration with Animal Research

As outlined in Chapters 2 and 3, it is difficult to directly compare EE research in laboratory animals to humans, due to differences in EE definitions, types and durations, as well as differences in human and animal physiology and anatomy (McDonald et al., 2018; Queen et al., 2020). In particular for the current research, the durations of the EE were brief, making it difficult to compare to the long-term EE generally reported in animal research.

Typically, animals are provided with continuous cage enrichment, over periods of weeks to months. This continuous enrichment is less plausible in human studies with long-term enrichment being intensive and time-consuming. Research does demonstrate that long-term impoverishment in humans, especially in early life (e.g. living in an orphanage), can lead to detrimental health effects for humans including smaller brain volumes (Mackes et al., 2020), blunted physiological stress responses (McLaughlin et al., 2015), increased psychopathology (Zeanah et al., 2009), alterations of immune cell profiles (Reid et al., 2019) and changes to genes and white blood cell composition (Esposito et al., 2016). However, little research has investigated the long-term effects of enriching the environment in humans.

This thesis explored the effects of one-off 30-minute EE interventions, feasible for use in humans in short-term, stressful settings such as in waiting rooms and hospital rooms. These acute EE interventions may work differently to long term changes in the environment. Long-term EE may be useful in environments that are deprived, including retirement homes, where the residents are often confined to their rooms for long periods, with little enrichment and novelty.

The brief EE interventions in this thesis did find similar results to acute animal research. Acutely, EE increases corticosterone levels in rodents (Benaroya-Milshtein et al., 2004; Moncek et al., 2004) signifying an increase in stimulation, comparable to the thesis findings for music and landscape artworks. However, in animals, longer-term EE tends to lead to decreases in baseline corticosterone and lower responses to stress (Belz et al., 2003; Mesa-Gresa et al., 2016). Therefore, longer exposure to the EE interventions in humans may provide stronger effects, especially for the stress outcomes, where little significant findings were found across conditions in the studies in this thesis.

8.3.2 Paro as an Intervention for Wound Healing

The research in this thesis demonstrates that interacting with the Paro robot can lead to improvements in skin healing after a stressor; however, this was not seen for the other interventions, including music. One proposed reason is that, as well as sensory EE, Paro also provides a form of social EE through its companionship. It may be this social component of the Paro robot that is key to the beneficial effects on healing. Previous research has shown that social support with another human can lead to improved SBR from a tape-stripping wound (Robinson, Ravikulan et al., 2017), and therefore interaction with Paro may lead to similar effects.

The positive effects of Paro on healing might be due to the effects of the social bonding hormone, oxytocin. Oxytocin is a hormone that regulates social behaviour and stress responses in animals and humans (Gouin & Kiecolt-Glaser, 2011). More positive social interactions and higher quality relationships are associated with higher oxytocin levels (Gouin et al., 2010; Gouin & Kiecolt-Glaser, 2011). As well as being released due to social bonding, oxytocin can also be induced via skin activation from touch and tactile enrichment (IsHak et al., 2011; Uvnäs-Moberg et al., 2015). In particular, research demonstrates that stroking animals can lead to the activation of the oxytocin system which has downstream benefits for stress reduction (Beetz et al., 2012).

Increased oxytocin has been found to improve wound healing in both animals (İşeri et al., 2010) and humans (Gouin et al., 2010); and the administration of an oxytocin receptor antagonist can eliminate this relationship in animals (Detillion et al., 2004). This is because oxytocin can modulate the HPA axis response to stress (DeVries et al., 2007; İşeri et al., 2010). In particular, oxytocin can suppress the release of cortisol, which, as discussed in Chapter 2, can have deleterious effects on wound healing (IsHak et al., 2011). This may explain why social support interventions in animals (Glasper & DeVries, 2005; Pyter et al.,

2014; Vegas et al., 2012) and humans (Robinson, Ravikulan et al., 2017) can lead to improvements in wound healing rates. Thus, previous studies show that oxytocin has an important influence on the wound healing process and can buffer the stress-induced delays in healing.

Social and tactile interaction with Paro may have led to the release of oxytocin, which could account for the improvements in SBR. This postulated mechanism is in line with Vitalo and colleagues' (2009) findings that the beneficial effects of EE on burn healing rates in rats were similar to the effects of administering oxytocin. The nestlets promote nest-making, which is an important social bonding behaviour for rodents to prepare for their offspring. This suggests that the effects of nestlets on burn healing follow a similar mechanism to social bonding and enrichment.

However, one recent study contradicts this theory. Geva et al (2020) investigated the effects of touching Paro during thermal stimulation on pain, mood and salivary oxytocin levels. Those participants who interacted with Paro had decreased pain and salivary oxytocin, and increased happiness, compared to the control group. There was also an inverse relationship between the sense of connection the participants had with Paro and salivary oxytocin levels. This study therefore suggests that interacting with Paro actually decreases oxytocin, contrary to hypotheses. However, this is the only study to have investigated the effects of Paro on oxytocin and given the difficulties in assessing oxytocin (McCullough et al., 2013) more research is needed on whether Paro can induce the production of oxytocin.

Study 2 found that the relationship between Paro and improved SBR was mediated by enjoyment levels, rather than a reduction in stress, which concurs with research showing that positive emotional states can lead to improved wound healing in humans (Ebrecht et al.,

2004; Robles et al., 2009). Although enjoyment itself is less studied as an important predictor of improved health and healing, it is an area future research could investigate further.

Paro had an effect on SBR in a stressed sample (Study 2), but not in a non-stressed sample (Study 1), which concurs with research in psychoneuroimmunology suggesting that stress-reduction interventions will have the greatest effects in stressed populations (G. E. Miller & Cohen, 2001). Stress has deleterious effects on immune functioning, and therefore interventions to reduce stress should be able to reverse these negative effects. In non-stressed populations, the immune system is functioning well and therefore, there is no need for an intervention to improve wound healing, as this process is not usually impaired. This theory supports the oxytocin mechanism described above. Oxytocin improves wound healing by suppressing the effects of cortisol, which has negative effects on various stages of wound healing (İşeri et al., 2010; IsHak et al., 2011). Therefore, in non-stressed people with low levels of cortisol, there may be a floor effect whereby the effects of oxytocin on cortisol are redundant. So, the use of Paro as an EE intervention for wound healing may only be appropriate in stressed individuals and the benefits may not generalise to non-stressed people.

The beneficial effects of Paro on SBR suggests that interacting with Paro may also affect psoriasis outcomes and a pilot study (Study 3) was conducted with this population. Moderate effect sizes were observed, which inform a full randomised controlled trial. These effects may become statistically significant in a fully powered study, although a one-off 30-minute EE intervention may be too brief to have an effect on psoriasis, as a beneficial effect may not be observable in a slowly responding condition over a short period. Previous research investigating the effects of psychological interventions on psoriasis used long-term interventions, usually over weeks to months (Lavda et al., 2012). Study 3 was the first study to investigate the effects of a brief, 30-minute psychological intervention on skin outcomes in psoriasis patients.

Therefore, the research in this thesis suggests that brief interactions with Paro are beneficial for short-term skin healing processes in stressed populations, but not necessarily for long-term skin disease. Future studies that are sufficiently powered to detect differences are needed once the intervention is optimised. Ways to administer Paro over a longer period could be investigated in future feasibility studies. Due to Paro's high cost, less expensive companion robots could be more feasible for long-term use for individuals at home. There may also be moderating effects of long-term loneliness, companionship and stress that need to be further investigated.

8.3.3 Music and Artwork as Stimulation

EE in the form of listening to music and viewing landscape artworks were found to be stimulating, as opposed to relaxing and stress-reducing. Despite being unexpected, this finding does agree with the existing research on EE. For example, in animal studies, EE has been found to improve learning and memory (J. C. Bennett et al., 2006; Schrijver et al., 2002), improve cognitive functioning (Sampedro-Piquero & Begega, 2016), and reduce the negative effects of aging and neurological disorders (Faherty et al., 2005; Fernández-Teruel et al., 2002; Mazarakis et al., 2014). Therefore, the stimulating aspect of EE may improve cognitive outcomes, and could still be important for wellbeing when applied to a human setting.

The stimulating effects of EE can be beneficial for health in both animals and humans. Many laboratory animals live in unstimulating environments and therefore these effects from EE are expected. Most humans live in stimulating environments, but further stimulation through EE can be useful in certain situations. For example, in humans different forms of EE, including multisensory stimulation, have been shown to improve cognitive functioning and wellbeing in patient groups including: stroke patients (Khan et al., 2016), older adults (De

Oliveira et al., 2014), autistic children (Weitlauf et al., 2017), patients with intellectual disabilities (De Giorgio, 2017), and patients with traumatic brain injuries (Frasca et al., 2013). Environmental stimulation throughout life has been shown to reduce to the cognitive deficits from aging (Cassarino & Setti, 2015). Therefore, in both animals and humans, the provision of EE can stimulate the brain and improve cognitive and neurological outcomes.

The duration of EE is an important moderating variable that may influence psychological responses. In the current research, the short-term stimulation caused by music and landscape artworks may be due to positive distraction. In the experimental studies of this thesis, the intervention period consisted of 30 minutes of interaction with different forms of EE or a control group. 30 minutes in a laboratory setting, with little other stimulation, may have led to an increase in boredom in participants. In contrast, the artworks and the music may have distracted participants from this boredom as the interventions captured participants' attention. Although not necessarily decreasing stress levels, these interventions could be stimulating enough to distract participants from negative experiences and boredom.

Timing is also an important moderating variable in this research. It is important to note that the stress task was finished by the time the participants were introduced to the EE interventions, and thus all participants' stress levels reduced over the intervention periods. Had the EE interventions been introduced earlier, while participants were still under stress from the TSST, then the effects of EE on the stress outcomes may have been stronger.

The scoping review suggests other possible moderators of the effects of viewing artwork on physiology, including the context the artwork is viewed in, individual differences, the content of the artwork, availability of choice, and the viewing directives provided. Stress levels may be an important moderator. In individuals facing a stressor, viewing artwork may lead to stress-reduction due to the positive distraction from their current stress levels.

Whereas in individuals who are not facing a stressor, viewing artwork may instead lead to stimulation. These possible moderators need to be researched in more detail, with rigorous studies, to determine the situations where viewing artwork is stimulating or stress-reducing, so that it can be used appropriately in clinical practice. The reduction in stress found in the scoping review suggests that viewing artwork could improve wound healing in populations currently undergoing a stressor, however no research has yet to explore this possibility.

Music may also be able to improve healing in stressed populations, if the timing is right. A recent meta-analysis has shown that listening to music reliably decreases both psychological and physiological stress outcomes (de Witte et al., 2019). These effects are theorised to be due to positive distraction (Kemper & Danhauer, 2005), modulation of emotions (de Witte et al., 2019) and direct physiological entrainment to the rhythm of the music (Yehuda, 2011). Based on these stress-reduction findings, music should also be able to improve wound healing rates. However, Studies 1 and 2 in this thesis are the only studies to have investigated the effects of music on wound healing. They did not find any beneficial effects, perhaps due to the timing of the intervention (after rather than during a stressor) or the type of wound. More research is required to further explore this possibility.

8.4 Clinical Implications

The findings from these four studies have clinical implications because EE for humans is an easy, simple and low-cost intervention with minimal, if any, negative effects. In particular, the EE interventions used were brief, one-off, 30-minute interventions, and therefore require little long-term involvement and commitment. These interventions could therefore be used in various settings and with different patient groups to improve stimulation and wound healing.

Sensory EE interventions could be particularly useful in sensorially deprived and impoverished environments, such as hospital rooms, waiting rooms, offices and retirement

homes. Individuals may be exposed to these unstimulating and inherently stressful environments for long periods of time. It is difficult for hospital patients or retirement home residents, who are often physically or cognitively limited and sedentary, to access EE themselves. Therefore, enriching these environments with simple EE interventions could have benefits by decreasing stress levels and improving stimulation. It has been suggested that due to the beneficial effects, EE in these different settings should be a standard, rather than an additional intervention (Janssen et al., 2010). The evidence from this thesis supports the literature that suggests these settings should have the addition of EE, such as artworks, as standard practice. Some retirement homes already use Paro with individuals with dementia and include artworks in common areas.

It is an important finding that the Paro robot can improve skin healing after a stressor because many patient groups are at risk of poor wound healing. For example, any intervention that can improve wound healing rates is particularly important in surgical patients as this could decrease risk of complications including infection, and decrease hospital stay lengths (Broadbent & Koschwanez, 2012). The benefit is not only for the patient, but also for the healthcare system due to decreased cost. A simple and brief EE intervention that has been shown to improve experimental healing, such as the Paro robot, can easily be introduced to patients either before or after surgery to help improve their surgical wound healing rates. The Paro robot also has anti-bacterial fur, and can be safely cleaned, so it can be used sanitarily within hospital contexts and by different patients (Aminuddin et al., 2016).

The findings for improved SBR, discussed in Chapter 5, are also important for people with dermatological disease where the skin barrier is impaired. Inflammatory skin disorders, such as psoriasis, are often exacerbated by stress. Therefore, interventions that can reduce stress or increase positive affect could improve clinical outcomes (Stewart et al., 2018). Although

Study 3 did not find any significant effects across condition in people with psoriasis, the findings were in hypothesised direction and future research could be conducted with Paro in the longer-term, with greater numbers of participants.

The Paro robot may also be beneficial for older adults in retirement homes. Retirement homes can be impoverished environments and older adults are more sedentary and lonelier than the general public, leading to a need for enrichment and companionship (Volkers & Scherder, 2011). Additionally, older adults are at greater risk for poor wound healing for many different reasons including loss of immune function, skin fragility, immobility and poorer nutrition (Schneiderman et al., 2005). Paro is well-accepted in this age group, and a large body of literature supports the effect of Paro decreasing stress in older adults, including promising results for decreasing sAA (Nomura & Hoshina, 2017), and urinary stress hormones (Saito et al., 2003), and increasing mood (Wada et al., 2006). Future research could specifically investigate the effects of Paro on wound healing in older adults to further corroborate these findings.

The research within this thesis also demonstrated improved stimulation from listening to music and viewing artwork. The stimulating aspects of EE may not be necessarily be beneficial for wound healing, but it is beneficial for other important aspects of health, such as cognitive and neurological functioning, wellbeing, behaviour and mood. Music could be particularly beneficial for patients with neurological disorders, such as dementia, autism and intellectual disabilities. In these patients, stimulation through EE has been shown to reduce aggression, confusion and symptoms (Woo et al., 2015). Dementia patients in particular benefit from music or artworks because these forms of EE can stimulate positive memories, thereby improving mood and wellbeing (Jakob & Collier, 2017). Therefore, for specific patient groups, stimulation from certain types of EE is beneficial for outcomes other than stress and wound healing.

Stimulation from EE may also be beneficial as a form of positive distraction from negative experiences and emotions. This could be particularly relevant for patients waiting for stressful and anxiety producing surgical or dental procedures. Stimulating music and/or artworks could be provided within waiting rooms to help distract them from anticipatory stress and anxiety. This could also have downstream benefits for their wound healing and recovery. Evidence suggest that there are positive effects of music in dental waiting rooms on anxiety (Thoma et al., 2015), and a beneficial effect on HR with a nature mural placed in a dental waiting room (Heerwagen, 1990). However, no research has investigated the effects of the addition of either music or artworks in waiting rooms on healing and recovery outcomes.

8.5 Limitations and Future Research

This research used novel methods to investigate the effects of EE in humans. However, important limitations of this research should be mentioned. Some limitations have already been discussed in the original manuscripts, however, an overview of the more general limitations of the studies is discussed below.

Firstly, the studies all used an experimental methodology in a laboratory setting. Although this leads to experimental control and lack of potential confounds, this can also lead to low ecological validity and clinical applicability. The procedures used within the studies were also experimental. For example, the wounding technique used in Studies 1 and 2 was an experimental tape-stripping wound, which may not directly represent the healing of a clinical wound. The tape-stripping wound is relatively minor and only causes a small disruption to the barrier of the skin. Clinical and surgical wounds, on the other hand, are more invasive and disrupt the deeper skin structures. These wounds therefore heal over a longer time-period, through a broader and more complicated wound healing trajectory. Therefore, it is difficult to directly generalise the healing results of Studies 1 and 2 to the healing of chronic or surgical

wounds. However, this experimental wounding procedure allows preliminary insight into how EE may affect simple wound healing processes, without the confounds of clinical wounds. Future research should investigate the effects of EE in samples with surgical or chronic wounds, or with more complex experimental wounding techniques, such as blister wounds or punch biopsies, to further investigate the generalisability of this research.

As well this, Studies 2, 3 and 4 used experimentally produced stress, through the TSST, which may not directly represent naturalistic stress. Despite the research that demonstrates that the TSST reliability increases both physiological and psychological stress (Allen et al., 2014), this is acute stress, rather than chronic stress. As discussed in Chapter 2, acute and chronic stress have different effects on the immune system and therefore will affect wound healing processes differently. Often, acute stress can actually be immuno-enhancing and improve wound healing rates (Dhabhar, 2014). Therefore, it cannot be concluded that the TSST caused an impairment in immune function or wound healing. Future research could investigate these procedures in participants who are already chronically stressed to remove the experimental and acute approach.

The diversity of the studies' participants was restricted, thereby limiting the generalisability of the effects found. Three of the studies were conducted on healthy, young samples, recruited mainly from a student population. Healthy samples allow for a reduction in confounds due to clinical comorbidities, but it makes it difficult to generalise these results to clinical disease. This is particularly important for patients with impaired immune systems, including older adults or people with comorbidities, who are both at risk of higher negative repercussions from stress and poor wound healing. Participants from Study 1 also had low levels of clinical stress and therefore, Study 2 had to experimentally stress the sample to focus on the stress-reducing effects of EE.

Study 3 attempted to address this limitation by recruiting a sample of patients with the skin disease psoriasis. Although these participants were more diverse and included a larger age range than the healthy samples, only 25 people were able to be recruited for this study due to recruitment issues and suspension of clinical research during COVID-19 lockdowns. Therefore, the studies within this thesis are unable to be generalised to patients with psoriasis without further research. As the Raman method has now been established, future research should investigate the effects of these EE interventions in larger samples, in other skin diseases such as atopic eczema or operative surgical recovery samples.

Another limitation of the experimental studies was that they only included one-off, short-term (30-minute) EE interventions. Longer interactions with the EE may have led to different psychological and physiological effects and future research could examine these long-term effects. Long-term interaction with Paro may lead to strengthened social bonds and therefore larger effects (Randall et al., 2019). The scoping review included longer-term research, so that the long-term effects of viewing artwork on stress-reduction can be interpreted. However, more research on this is needed to further determine the dose-response relationship.

The research in this thesis did not give participants a choice of which EE they wanted to engage with. As discussed in the introduction chapters, choice is a key feature of EE, especially for humans who have the extra factor of motivation (Frasca et al., 2013). Although the music condition did have a choice of what type of music to listen to from a selection of CDs, the other conditions did not have any aspect of choice. More naturalistic research in EE tends to provide multiple types of EE, and patients are able to choose interventions. For example, the research for enriching stroke units provides stroke patients with various types of EE (including games, books and artwork) and the patient has a choice of whether they want interact with the EE items (Janssen et al., 2014; Khan et al., 2016; Rosbergen et al., 2017; J.

H. White et al., 2015). Removing this aspect of choice may have limited the effects that were reported in the research.

Not every type of EE will be effective for every person and EE may need to be tailored to the individual. For example, research has shown that there are large individual variations in responses to Paro (Kang et al., 2020). In the current research, most participants enjoyed interacting with Paro; however, not all participants liked it and some informally reported that it was “creepy”, “disturbing” or they were just not interested in it. Therefore, for these individuals, there would be limited social connections formed with Paro and limited increases in enjoyment, resulting in the beneficial effects on healing being blunted. It is probable that interacting with Paro only has beneficial effects in those who enjoy the interaction. However, the research in this thesis did not quantify the participants’ feelings about Paro, therefore this potential moderator was not explored. Future research should investigate whether the individuals’ perceptions of Paro affect the SBR results.

The aspect of choice was detected as a possible moderator in the scoping review for viewing artworks. Giving patients choice over the type of artwork they view may provide them with a sense of control over their environment. Although in clinical practice, patients in hospitals can be provided with a choice of artwork to view through the provision of Art Carts (Suter & Baylin, 2007), little empirical research has been conducted in this area, as most artwork studies provide patients with pre-determined artworks. Future research could focus on multiple EE interventions and provide the participants with a choice of interventions with which they would like to engage.

Due to the exploratory nature of this thesis and the large variety in available EE types, this thesis only focused on a small number of EE interventions. There are many other EE interventions for humans that could be explored further to examine their effects on stress and

wound healing including: social support, nature exposure, virtual reality, changes in colour or lighting, other auditory additions, such as nature sounds, and sensory integration therapy or multi-sensory stimulation programmes. Although some research has been conducted on these types of EE, future research could further explore the effects of these EE interventions on stress and wound healing outcomes.

8.6 Conclusions

Using four experimental studies and a scoping review, this thesis explored possible EE interventions to improve skin healing and stress in humans. The key findings were that although some EE interventions, such as the Paro robot, can increase enjoyment and improve skin healing rates, other EE interventions, such as artwork and music, may instead increase stimulation levels which may not influence healing processes, at least in the short-term. Paro is different from the other forms of EE investigated because it is a form of social enrichment, which may make it particularly effective. A key difference in this research compared to previous long-term research with animals, is the shorter duration of the EE provided. Longer-term interventions still need to be studied in humans. Both increases in stimulation and improvements in skin healing rates are important outcomes for different reasons and populations. Careful consideration of the choice of EE intervention is important in human research, depending on the desired outcomes. This work is a novel addition to the literature as until this thesis no research had been conducted investigating the effects of EE in humans on wound healing outcomes. Future research could explore these findings in patients with clinical wounds and further examine the possible moderators that make EE in humans relaxing or stimulating. This thesis therefore provides preliminary findings and guidance for further research on the effects of EE on stress and healing in humans.

References

Allen, A. P., Kennedy, P. J., Cryan, J. F., Dinan, T. G., & Clarke, G. (2014). Biological and psychological markers of stress in humans: focus on the Trier Social Stress Test. *Neuroscience & Biobehavioral Reviews*, *38*, 94-124. https://doi.org/10.1016/j.neubiorev.2013.11.005

Altemus, M., Rao, B., Dhabhar, F. S., Ding, W., & Granstein, R. D. (2001). Stress-induced changes in skin barrier function in healthy women. *Journal of Investigative Dermatology*, *117*(2), 309-317. https://doi.org/10.1046/j.1523-1747.2001.01373.x

Aminuddin, R., & Sharkey, A. (2017). A Paro robot reduces the stressful effects of environmental noise. In *Proceedings of the European Conference on Cognitive Ergonomics 2017* (pp. 63-64). Association for Computing Machinery https://doi.org/10.1145/3121283.3121420

Aminuddin, R., Sharkey, A., & Levita, L. (2016). Interaction with the Paro robot may reduce psychophysiological stress responses. In *2016 11th ACM/IEEE International Conference on Human-Robot Interaction* (pp. 593-594). IEEE. https://doi.org/10.1109/HRI.2016.7451872.

Aronoff, E., Hillyer, R., & Leon, M. (2016). Environmental enrichment therapy for autism: outcomes with increased access. *Neural Plasticity*, *2016*, 1-23. https://doi.org/10.1155/2016/2734915

Arranz, L., De Castro, N. M., Baeza, I., Maté, I., Viveros, M. P., & De la Fuente, M. (2010). Environmental enrichment improves age-related immune system impairment: Long-term exposure since adulthood increases life span in mice. *Rejuvenation Research*, *13*(4), 415-428. http://doi.org/10.1089/rej.2009.0989

Aston-Jones, G., & Cohen, J. D. (2005). An integrative theory of locus coeruleus-norepinephrine function: Adaptive gain and optimal performance. *Annual Review of Neuroscience*, *28*, 403-450. https://doi.org/10.1146/annurev.neuro.28.061604.135709

Beetz, A., Uvnäs-Moberg, K., Julius, H., & Kotrschal, K. (2012). Psychosocial and psychophysiological effects of human-animal interactions: the possible role of oxytocin. *Frontiers in Psychology*, *3*, 234. https://doi.org/10.3389/fpsyg.2012.00234

Belz, E. E., Kennell, J. S., Czambel, R. K., Rubin, R. T., & Rhodes, M. E. (2003). Environmental enrichment lowers stress-responsive hormones in singly housed male and female rats. *Pharmacology Biochemistry and Behavior*, *76*(3), 481-486. https://doi.org/10.1016/j.pbb.2003.09.005

Benaroya-Milshtein, N., Apter, A., Yaniv, I., Kukulansky, T., Raz, N., Haberman, Y., Halpert, H., Pick, C. G., & Hollander, N. (2007). Environmental enrichment augments the efficacy of idiotype vaccination for B-cell lymphoma. *Journal of Immunotherapy*, *30*(5), 517-522. https://doi.org/10.1097/CJI.0b013e31804efc5e

Benaroya-Milshtein, N., Hollander, N., Apter, A., Kukulansky, T., Raz, N., Wilf, A., Yaniv, I., & Pick, C. G. (2004). Environmental enrichment in mice decreases anxiety, attenuates stress responses and enhances natural killer cell activity. *European Journal of Neuroscience*, *20*(5), 1341-1347. https://doi.org/10.1111/j.1460-9568.2004.03587.x

Bennett, C. C., Sabanovic, S., Piatt, J. A., Nagata, S., Eldridge, L., & Randall, N. (2017). A robot a day keeps the blues away. In *2017 IEEE International Conference on Healthcare Informatics* (pp. 536-540). IEEE. https://doi.org/10.1109/ICHI.2017.4

Bennett, J. C., McRae, P. A., Levy, L. J., & Frick, K. M. (2006). Long-term continuous, but not daily, environmental enrichment reduces spatial memory decline in aged male mice. *Neurobiology of Learning and Memory*, *85*(2), 139-152. https://doi.org/10.1016/j.nlm.2005.09.003

Berman, M. G., Jonides, J., & Kaplan, S. (2008). The cognitive benefits of interacting with nature. *Psychological Science*, *19*(12), 1207-1212. https://doi.org/10.1111/j.1467-9280.2008.02225.x

Bice, B. D., Stephens, M. R., Georges, S. J., Venancio, A. R., Bermant, P. C., Warncke, A. V., Affolter, K. E., Hidalgo, J. R., & Angus-Hill, M. L. (2017). Environmental enrichment induces pericyte and IgA-dependent wound repair and lifespan extension in a colon tumor model. *Cell Reports*, *19*(4), 760-773. https://doi.org/10.1016/j.celrep.2017.04.006

Binnie, J. (2010). Does viewing art in the museum reduce anxiety and improve wellbeing? *Museums & Social Issues*, *5*(2), 191-201. https://doi.org/10.1179/msi.2010.5.2.191

Boyce, M., Bungay, H., Munn-Giddings, C., & Wilson, C. (2018). The impact of the arts in healthcare on patients and service users: A critical review. *Health & Social Care in the Community*, *26*(4), 458-473. https://doi.org/10.1111/hsc.12502

Broadbent, E., Kahokehr, A., Booth, R. J., Thomas, J., Windsor, J. A., Buchanan, C. M., Wheeler, B. R. L., Tarik, S., & Hill, A. G. (2012). A brief relaxation intervention reduces stress and improves surgical wound healing response: A randomised trial. *Brain, Behavior, and Immunity*, *26*(2), 212-217. https://doi.org/10.1016/j.bbi.2011.06.014

Broadbent, E., & Koschwanez, H. E. (2012). The psychology of wound healing. *Current Opinion in Psychiatry*, *25*(2), 135-140. https://doi.org/10.1097/YCO.0b013e32834e1424

Broadbent, E., Petrie, K. J., Alley, P. G., & Booth, R. J. (2003). Psychological stress impairs early wound repair following surgery. *Psychosomatic Medicine*, *65*(5), 865-869. http://doi.org/10.1097/01.PSY.0000088589.92699.30

Brod, S., Gobbetti, T., Gittens, B., Ono, M., Perretti, M., & D'Acquisto, F. (2017). The impact of environmental enrichment on the murine inflammatory immune response. *JCI Insight*, *2*(7), e90723. http://doi.org/10.1172/jci.insight.90723

Brown, D. K., Barton, J. L., & Gladwell, V. F. (2013). Viewing nature scenes positively affects recovery of autonomic function following acute-mental stress. *Environmental Science & Technology*, *47*(11), 5562-5569. https://doi.org/10.1021/es305019p

Bundy, C., Pinder, B., Bucci, S., Reeves, D., Griffiths, C. E. M., & Tarrier, N. (2013). A novel, web-based, psychological intervention for people with psoriasis: The electronic Targeted Intervention for Psoriasis (eTIP s) study. *British Journal of Dermatology*, *169*(2), 329-336. https://doi.org/10.1111/bjd.12350

Buske-Kirschbaum, A., Kern, S., Ebrecht, M., & Hellhammer, D. H. (2007). Altered distribution of leukocyte subsets and cytokine production in response to acute psychosocial stress in patients with psoriasis vulgaris. *Brain, Behavior, and Immunity*, *21*(1), 92-99. https://doi.org/10.1016/j.bbi.2006.03.006

Bygren, L. O., Birgitta, N. Wikström, B., Konlaan, B. B., Karlsson, A., Elgh, E., Grjibovski, A. M., & Sandström, S. (2013). Seniors' experiences of visual art environmental enrichment. *Open Journal of Nursing*, *3*(2), 163-168. https://doi.org/10.4236/ojn.2013.32021

Carswell, C., Reid, J., Walsh, I., & Noble, H. (2018). Arts-based interventions for hospitalised patients with cancer: A systematic literature review. *British Journal of Healthcare Management*, *24*(12), 611-616. https://doi.org/10.12968/bjhc.2018.24.12.611

Cassarino, M., & Setti, A. (2015). Environment as 'brain training': A review of geographical and physical environmental influences on cognitive ageing. *Ageing Research Reviews*, *23*, 167-182. https://doi.org/10.1016/j.arr.2015.06.003

Chafin, S., Roy, M., Gerin, W., & Christenfeld, N. (2004). Music can facilitate blood pressure recovery from stress. *British Journal of Health Psychology*, *9*(3), 393-403. https://doi.org/10.1348/1359107041557020

Chang, C. Y. (2002). Psychophysiological responses to different landscape settings and a comparison of cultural differences. In *XXVI International Horticultural Congress: Expanding Roles for Horticulture in Improving Human Well-Being and Life Quality 639* (pp. 57-65). http://doi.org/10.17660/ActaHortic.2004.639.6

Chang, W. L., Šabanovic, S., & Huber, L. (2013). Use of seal-like robot PARO in sensory group therapy for older adults with dementia. In *2013 8th ACM/IEEE International Conference on Human-Robot Interaction* (pp. 101-102). IEEE. http://doi.org/10.1109/HRI.2013.6483521

Chapman, B. P., & Moynihan, J. (2009). The brain–skin connection: Role of psychosocial factors and neuropeptides in psoriasis. *Expert Review of Clinical Immunology*, *5*(6), 623-627. https://doi.org/10.1586/eci.09.56

Charmandari, E., Tsigos, C., & Chrousos, G. (2005). Endocrinology of the stress response. *Annual Review of Physiology*, *67*, 259-284. https://doi.org/10.1146/annurev.physiol.67.040403.120816

Chen, Y., & Lyga, J. (2014). Brain-skin connection: stress, inflammation and skin aging. *Inflammation & Allergy-Drug Targets*, *13*(3), 177-190. https://doi.org/10.2174/1871528113666140522104422

Chen, Y., Xin, T., & Cheng, A. S. (2014). Evaluating the effectiveness of psychological and/or educational interventions in psoriasis: A narrative review. *The Journal of Dermatology*, *41*(9), 775-778. https://doi.org/10.1111/1346-8138.12583

Christian, L. M., Graham, J. E., Padgett, D. A., Glaser, R., & Kiecolt-Glaser, J. K. (2006). Stress and wound healing. *Neuroimmunomodulation*, *13*(5-6), 337-346. http://doi.org/10.1159/000104862

Clemenson, G. D., Deng, W., & Gage, F. H. (2015). Environmental enrichment and neurogenesis: From mice to humans. *Current Opinion in Behavioral Sciences*, *4*, 56-62. https://doi.org/10.1016/j.cobeha.2015.02.005

Clemenson, G. D., & Stark, C. E. (2015). Virtual environmental enrichment through video games improves hippocampal-associated memory. *Journal of Neuroscience*, *35*(49), 16116-16125. https://doi.org/10.1523/JNEUROSCI.2580-15.2015

Clemenson, G. D., Stark, S. M., Rutledge, S. M., & Stark, C. E. (2020). Enriching hippocampal memory function in older adults through video games. *Behavioural Brain Research*, *390*, 112667. https://doi.org/10.1016/j.bbr.2020.112667

Clow, A., & Fredhoi, C. (2006). Normalisation of salivary cortisol levels and self-report stress by a brief lunchtime visit to an art gallery by London City workers. *Journal of Holistic Healthcare*, *3*(2), 29-32.

Cohen, S., Janicki-Deverts, D., & Miller, G. E. (2007). Psychological stress and disease. *JAMA*, *298*(14), 1685-1687. https://doi.org/10.1001/jama.298.14.1685

Cohen, S., Kamarck, T., & Mermelstein, R. (1994). Perceived stress scale. *Measuring Stress: A Guide for Health and Social Scientists*, *10*, 1-2.

Cohen, S., & Pressman, S. D. (2006). Positive affect and health. *Current Directions in Psychological Science, 15*(3), 122-125. https://doi.org/10.1111/j.0963-7214.2006.00420.x

Cohen, S., & Williamson, G. M. (1991). Stress and infectious disease in humans. *Psychological Bulletin*, *109*(1), 5-24. https://doi.org/10.1037/0033-2909.109.1.5

Coleman, K., Weed, J. L., & Schapiro, S. J. (2013). Environmental enrichment for animals used in research. In P. Michael Conn (Ed.) *Animal Models for the Study of Human Disease* (pp. 75-94). Academic Press. https://doi.org/10.1016/B978-0-12-415894-8.00004-X

Coleman, K., Weed, J. L., & Schapiro, S. J. (2017). Psychological environmental enrichment of animals in research. In P. Michael Conn (Ed.) *Animal Models for the Study of Human Disease (Second Edition)* (pp. 47-69). Academic Press. https://doi.org/10.1016/B978-0-12-809468-6.00002-4

Corcoran, C., Walker, E., Huot, R., Mittal, V., Tessner, K., Kestler, L., & Malaspina, D. (2003). The stress cascade and schizophrenia: Etiology and onset. *Schizophrenia Bulletin*, *29*(4), 671-692. https://doi.org/10.1093/oxfordjournals.schbul.a007038

Crofton, E. J., Zhang, Y., & Green, T. A. (2015). Inoculation stress hypothesis of environmental enrichment. *Neuroscience and Biobehavioral Reviews, 49*, 19-31. https://doi.org/10.1016/j.neubiorev.2014.11.017

Curtis, W. J., & Nelson, C. A. (2003). Towards building a better brain: Neuro-behavioral outcomes, mechanisms and processes of environment enrichment. In D. Cicchetti (Ed.) *Resilience and Vulnerability: Adaptation in the Context of Childhood Adversities*, (pp. 463-488). Cambridge University Press. https://doi.org/10.1017/CBO9780511615788.021

Dandi, E., Kalamari, A., Touloumi, O., Lagoudaki, R., Nousiopoulou, E., Simeonidou, C., Spandou, E., & Tata, D. A. (2018). Beneficial effects of environmental enrichment on behavior, stress reactivity and synaptophysin/BDNF expression in hippocampus following early life stress. *International Journal of Developmental Neuroscience*, *67*, 19-32. https://doi.org/10.1016/j.ijdevneu.2018.03.003

Davies, C. R., Rosenberg, M., Knuiman, M., Ferguson, R., Pikora, T., & Slatter, N. (2012). Defining arts engagement for population-based health research: Art forms, activities and level of engagement. *Arts & Health*, *4*(3), 203-216. https://doi.org/10.1080/17533015.2012.656201

Daykin, N., Byrne, E., Soteriou, T., & O'Connor, S. (2008). Review: The impact of art, design and environment in mental healthcare: A systematic review of the literature. *Journal of the Royal Society for the Promotion of Health, 128*(2), 85-94. https://doi.org/10.1177/1466424007087806

D'Cunha, N. M., McKune, A. J., Isbel, S., Kellett, J., Georgousopoulou, E. N., & Naumovski, N. (2019). Psychophysiological responses in people living with dementia after an art gallery intervention: An exploratory study. *Journal of Alzheimer's Disease*, *72*(2), 549-562. https://doi.org/10.3233/JAD-190784

de Azevedo, C. S., Cipreste, C. F., & Young, R. J. (2007). Environmental enrichment: A GAP analysis. *Applied Animal Behaviour Science, 102*(3-4), 329-343. https://doi.org/10.1016/j.applanim.2006.05.034

De Giorgio, A. (2017). The roles of motor activity and environmental enrichment in intellectual disability. *Somatosensory & Motor Research*, *34*(1), 34-43. https://doi.org/10.1080/08990220.2016.1278204

de Jong, M. A. (1972). A physiological approach to aesthetic preference–I. Paintings. *Psychotherapy and Psychosomatics*, *20*(6), 360-365. https://doi.org/10.1159/000286439

De la Fuente, M., & Arranz, L. (2012). The importance of the environment in brain aging: Be happy, live longer! In M. Thakur & S. Rattan (Eds.) *Brain Aging and Therapeutic Interventions* (pp. 79-94). Springer. https://doi.org/10.1007/978-94-007-5237-5_6

de la O-Cuevas, E., Badillo-Ramírez, I., Islas, S. R., Araujo-Andrade, C., & Saniger, J. M. (2019). Sensitive Raman detection of human recombinant interleukin-6 mediated by DCDR/GERS hybrid platforms. *RSC Advances*, *9*(22), 12269-12275. https://doi.org/10.1039/C9RA01396B

De Oliveira, T. C. G., Soares, F. C., De Macedo, L. D. E. D., Diniz, D. L. W. P., Bento-Torres, N. V. O., & Picanço-Diniz, C. W. (2014). Beneficial effects of multisensory and cognitive stimulation on age-related cognitive decline in long-term-care institutions. *Clinical Interventions in Aging*, *9*, 309. http://doi.org/10.2147/CIA.S54383

de Sousa, A. A., Reis, R., Bento-Torres, J., Trévia, N., de Almeida Lins, N. A., Passos, A., Santos, Z., Picanço Diniz, J. A., da Costa Vasconcelos, P. F., Cunningham, C., Perry, V. H., & Picanço Diniz, C. W. (2011). Influence of enriched environment on viral encephalitis outcomes: Behavioral and neuropathological changes in albino Swiss mice. *PloS One*, *6*(1), e15597. https://doi.org/10.1371/journal.pone.0015597

de Witte, M., Spruit, A., van Hooren, S., Moonen, X., & Stams, G. J. (2019). Effects of music interventions on stress-related outcomes: A systematic review and two meta-analyses. *Health Psychology Review*, *14*(2), 294-324. https://doi.org/10.1080/17437199.2019.1627897

Denda, M., Sokabe, T., Fukumi-Tominaga, T., & Tominaga, M. (2007). Effects of skin surface temperature on epidermal permeability barrier homeostasis. *Journal of Investigative Dermatology*, *127*(3), 654-659. https://doi.org/10.1038/sj.jid.5700590

Detillion, C. E., Craft, T. K., Glasper, E. R., Prendergast, B. J., & DeVries, A. C. (2004). Social facilitation of wound healing. *Psychoneuroendocrinology*, *29*(8), 1004-1011. https://doi.org/10.1016/j.psyneuen.2003.10.003

DeVries, A. C., Craft, T. K., Glasper, E. R., Neigh, G. N., & Alexander, J. K. (2007). 2006 Curt P. Richter award winner: social influences on stress responses and health. *Psychoneuroendocrinology*, *32*(6), 587-603. https://doi.org/10.1016/j.psyneuen.2007.04.007

Dhabhar, F. S. (2000). Acute stress enhances while chronic stress suppresses skin immunity: The role of stress hormones and leukocyte trafficking. *Annals of the New York Academy of Sciences*, *917*(1), 876-893. https://doi.org/10.1111/j.1749-6632.2000.tb05454.x

Dhabhar, F. S. (2014). Effects of stress on immune function: The good, the bad, and the beautiful. *Immunologic Research*, *58*(2), 193-210. https://doi.org/10.1007/s12026-014-8517-0

Dhabhar, F. S. (2019). The power of positive stress–A complementary commentary. *Stress*, *22*(5), 526-529. https://doi.org/10.1080/10253890.2019.1634049

Dickerson, S. S., & Kemeny, M. E. (2004). Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. *Psychological Bulletin*, *130*(3), 355. https://doi.org/10.1037/0033-2909.130.3.355

Dolivo, V., & Taborsky, M. (2017). Environmental enrichment of young adult rats (rattus norvegicus) in different sensory modalities has long-lasting effects on their ability to learn via specific sensory channels. *Journal of Comparative Psychology*, *131*(2), 79. https://doi.org/10.1037/com0000063

Ebrecht, M., Hextall, J., Kirtley, L., Taylor, A., Dyson, M., & Weinman, J. (2004). Perceived stress and cortisol levels predict speed of wound healing in healthy male adults. *Psychoneuroendocrinology*, *29*(6), 798-809. https://doi.org/10.1016/S0306-4530(03)00144-6

Eilers, P. H. (2003). A perfect smoother. *Analytical Chemistry*, *75*(14), 3631-3636. https://doi.org/10.1021/ac034173t

Eisen, S. L., Ulrich, R. S., Shepley, M. M., Varni, J. W., & Sherman, S. (2008). The stress-reducing effects of art in pediatric health care: Art preferences of healthy children and hospitalized children. *Journal of Child Health Care*, *12*(3), 173-190. https://doi.org/10.1177/1367493508092507

Ekstrand, J., Hellsten, J., & Tingström, A. (2008). Environmental enrichment, exercise and corticosterone affect endothelial cell proliferation in adult rat hippocampus and prefrontal cortex. *Neuroscience Letters*, *442*(3), 203-207. https://doi.org/10.1016/j.neulet.2008.06.085

Eming, S. A., & Tomic-Canic, M. (2017). Updates in wound healing: Mechanisms and translation. *Experimental Dermatology*, *26*(2), 97-98. https://doi.org/10.1111/exd.13281

Erckens, R. J., Motamedi, M., March, W. F., & Wicksted, J. P. (1997). Raman spectroscopy for non-invasive characterization of ocular tissue: Potential for detection of biological molecules. *Journal of Raman spectroscopy*, *28*(5), 293-299. https://doi.org/10.1002/(SICI)1097-4555(199705)28:5<293::AID-JRS47>3.0.CO;2-0

Esposito, E. A., Jones, M. J., Doom, J. R., MacIsaac, J. L., Gunnar, M. R., & Kobor, M. S. (2016). Differential DNA methylation in peripheral blood mononuclear cells in adolescents exposed to significant early but not later childhood adversity. *Development and Psychopathology*, *28*(4 Pt 2), 1385. https://doi.org/10.1017/S0954579416000055

Evans, J. D., Crooks, V. A., & Kingsbury, P. T. (2009). Theoretical injections: On the therapeutic aesthetics of medical spaces. *Social Science & Medicine*, *69*(5), 716-721. https://doi.org/10.1016/j.socscimed.2009.06.040

Faherty, C. J., Raviie Shepherd, K., Herasimtschuk, A., & Smeyne, R. J. (2005). Environmental enrichment in adulthood eliminates neuronal death in experimental parkinsonism. *Molecular Brain Research*, *134*(1), 170-179. https://doi.org/10.1016/j.molbrainres.2004.08.008

Fairhurst, G. D., Frey, M. D., Reichert, J. F., Szelest, I., Kelly, D. M., & Bortolotti, G. R. (2011). Does environmental enrichment reduce stress? An integrated measure of corticosterone from feathers provides a novel perspective. *PLoS One*, *6*(3), e17663. https://doi.org/10.1371/journal.pone.0017663

Fancourt, D., Ockelford, A., & Belai, A. (2014). The psychoneuroimmunological effects of music: A systematic review and a new model. *Brain, Behavior, and Immunity*, *36*, 15-26. https://doi.org/10.1016/j.bbi.2013.10.014

Fancourt, D., & Steptoe, A. (2019). Cultural engagement and mental health: Does socio-economic status explain the association? *Social Science & Medicine*, *236*, 112425. https://doi.org/10.1016/j.socscimed.2019.112425

Fancourt, D., Steptoe, A., & Cadar, D. (2018). Cultural engagement and cognitive reserve: Museum attendance and dementia incidence over a 10-year period. *The British Journal of Psychiatry*, *213*(5), 661-663. https://doi.org/10.1192/bjp.2018.129

Fancourt, D., & Tymoszuk, U. (2019). Cultural engagement and incident depression in older adults: Evidence from the English longitudinal study of ageing. *The British Journal of Psychiatry*, *214*(4), 225-229. https://doi.org/10.1192/bjp.2018.267

Faul, F., Erdfelder, E., Lang, A., & Buchner, A. (2007). G* power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, *39*(2), 175-191. https://doi.org/10.3758/BF03193146

Fernández-Teruel, A., Giménez-Llort, L., Escorihuela, R. M., Gil, L., Aguilar, R., Steimer, T., & Tobena, A. (2002). Early-life handling stimulation and environmental enrichment: Are some of their effects mediated by similar neural mechanisms? *Pharmacology Biochemistry and Behavior*, *73*(1), 233-245. https://doi.org/10.1016/S0091-3057(02)00787-6

Finn, S., & Fancourt, D. (2018). The biological impact of listening to music in clinical and nonclinical settings: A systematic review. *Progress in Brain Research*, *237*, 173-200. https://doi.org/10.1016/bs.pbr.2018.03.007

Flatt, J. D., & Hughes, T. F. (2013). Participation in social activities in later life: Does enjoyment have important implications for cognitive health? *Aging Health*, *9*(2), 149-158. https://doi.org/10.2217/ahe.13.11

Fluhr, J. W., & Darlenski, R. (2014). Transepidermal water loss (TEWL). In E. Berardesca, H. Maibach, & K. P. Wilhelm (Eds.), *Non invasive Diagnostic Techniques in Clinical Dermatology* (pp. 353-356). Springer. https://doi.org/10.1007/978-3-642-32109-2_32

Fordham, B., Griffiths, C. E., & Bundy, C. (2013). Can stress reduction interventions improve psoriasis? A review. *Psychology, Health & Medicine*, *18*(5), 501-514. https://doi.org/10.1080/13548506.2012.736625

Fordham, B., Griffiths, C. E. M., & Bundy, C. (2015). A pilot study examining mindfulness-based cognitive therapy in psoriasis. *Psychology, Health & Medicine*, *20*(1), 121-127. https://doi.org/10.1080/13548506.2014.902483

Fortune, D. G., Richards, H. L., Kirby, B., Bowcock, S., Main, C. J., & Griffiths, C. E. M. (2002). A cognitive-behavioural symptom management programme as an adjunct in psoriasis therapy. *British Journal of Dermatology*, *146*(3), 458-465. https://doi.org/10.1046/j.1365-2133.2002.04622.x

Fortune, D. G., Richards, H. L., Kirby, B., McElhone, K., Markham, T., Rogers, S., Main, C. J., & Griffiths, C. E. (2003). Psychological distress impairs clearance of psoriasis in

patients treated with photochemotherapy. *Archives of Dermatology*, *139*(6), 752-756. https://doi.org/10.1001/archderm.139.6.752

Fortune, D. G., Richards, H. L., Main, C. J., & Griffiths, C. E. (2000). Pathological worrying, illness perceptions and disease severity in patients with psoriasis. *British Journal of Health Psychology*, *5*(1), 71-82. https://doi.org/10.1348/135910700168775

Frasca, D., Tomaszczyk, J., McFadyen, B. J., & Green, R. E. (2013). Traumatic brain injury and post-acute decline: What role does environmental enrichment play? A scoping review. *Frontiers in Human Neuroscience*, *7*, 31. https://doi.org/10.3389/fnhum.2013.00031

Fredriksson, T., & Pettersson, U. (1978). Severe psoriasis–Oral therapy with a new retinoid. *Dermatology*, *157*(4), 238-244. https://doi.org/10.1159/000250839

Fricchione, J. G., & Levine, J. B. (2017). Deprived and enriched environments: How sensory stimulation affects wound healing. In M. L. Yarmush & A. Goldberg (Eds.), *Bioengineering in Wound Healing: A Systems Approach* (pp. 59-97). World Scientific. https://doi.org/10.1142/9789813144583_0003

Fries, E., Dettenborn, L., & Kirschbaum, C. (2009). The cortisol awakening response (CAR): Facts and future directions. *International Journal of Psychophysiology*, *72*(1), 67-73. https://doi.org/10.1016/j.ijpsycho.2008.03.014

Fukuda, S., Baba, S., & Akasaka, T. (2015). Psychological stress has the potential to cause a decline in the epidermal permeability barrier function of the horny layer. *International Journal of Cosmetic Science*, *37*(1), 63-69. https://doi.org/10.1111/ics.12169

Garg, A., Chren, M. M., Sands, L. P., Matsui, M. S., Marenus, K. D., Feingold, K. R., & Elias, P. M. (2001). Psychological stress perturbs epidermal permeability barrier homeostasis: Implications for the pathogenesis of stress-associated skin disorders. *Archives of Dermatology*, *137*(1), 53-59. https://doi.org/10.1001/archderm.137.1.53

Garofalo, S., D'Alessandro, G., Chece, G., Brau, F., Maggi, L., Rosa, A., Porzia, A., Mainiero, F., Esposito, V., Lauro, C., Benigni, G., Bernardini, G., Santoni, A., & Limatola, C. (2015). Enriched environment reduces glioma growth through immune and non-immune mechanisms in mice. *Nature Communications*, *6*(1), 1-13. https://doi.org/10.1038/ncomms7623

Geers, N. C., Zegel, M., Huybregts, J. G., & Niessen, F. B. (2018). The influence of preoperative interventions on postoperative surgical wound healing in patients without risk factors: A systematic review. *Aesthetic Surgery Journal*, *38*(11), 1237-1249. https://doi.org/10.1093/asj/sjy074

George, D. R., de Boer, C., & Green, M. J. (2017). "That landscape is where I'd like to be…": Offering patients with cancer a choice of artwork. *JAMA*, *317*(9), 890-892. http://doi.org/10.1001/jama.2017.1233

Geva, N., Uzefovsky, F., & Levy-Tzedek, S. (2020). Touching the social robot PARO reduces pain perception and salivary oxytocin levels. *Scientific Reports*, *10*(1), 1-15. https://doi.org/10.1038/s41598-020-66982-y

Gidron, Y. (2019). Effects of psychological predictors and interventions on recovery from surgery. In *Behavioral Medicine* (pp. 151-165). Springer. https://doi.org/10.1007/978-3-030-18893-1_9

Ginandes, C., Brooks, P., Sando, W., Jones, C., & Aker, J. (2003). Can medical hypnosis accelerate post-surgical wound healing? Results of a clinical trial. *American Journal of Clinical Hypnosis*, *45*(4), 333-351. https://doi.org/10.1080/00029157.2003.10403546

Girbovan, C., & Plamondon, H. (2013). Environmental enrichment in female rodents: Considerations in the effects on behavior and biochemical markers. *Behavioural Brain Research*, *253*, 178-190. https://doi.org/10.1016/j.bbr.2013.07.018

Gladwell, V. F., Brown, D. K., Barton, J. L., Tarvainen, M. P., Kuoppa, P., Pretty, J., Suddaby, J. M., & Sandercock, G. (2012). The effects of views of nature on autonomic control. *European Journal of Applied Physiology*, *112*(9), 3379-3386. https://doi.org/10.1007/s00421-012-2318-8

Glaser, R., & Kiecolt-Glaser, J. K. (2005). Stress-induced immune dysfunction: Implications for health. *Nature Reviews Immunology*, *5*(3), 243-251. https://doi.org/10.1038/nri1571

Glasper, E. R., & DeVries, A. C. (2005). Social structure influences effects of pair-housing on wound healing. *Brain, Behavior, and Immunity*, *19*(1), 61-68. https://doi.org/10.1016/j.bbi.2004.03.002

Goodman, W. K., Janson, J., & Wolf, J. M. (2017). Meta-analytical assessment of the effects of protocol variations on cortisol responses to the trier social stress test. *Psychoneuroendocrinology*, *80*, 26-35. https://doi.org/10.1016/j.psyneuen.2017.02.030

Goon, A. T., Yosipovitch, G., Chan, Y., & Goh, C. (2004). Barrier repair in chronic plaque-type psoriasis. *Skin Research and Technology*, *10*(1), 10-13. https://doi.org/10.1111/j.1600-0846.2004.00046.x

Gouin, J., Carter, C. S., Pournajafi-Nazarloo, H., Glaser, R., Malarkey, W. B., Loving, T. J., Stowell, J., & Kiecolt-Glaser, J. K. (2010). Marital behavior, oxytocin, vasopressin, and wound healing. *Psychoneuroendocrinology*, *35*(7), 1082-1090. https://doi.org/10.1016/j.psyneuen.2010.01.009

Gouin, J., & Kiecolt-Glaser, J. K. (2011). The impact of psychological stress on wound healing: Methods and mechanisms. *Immunology and Allergy Clinics of North America*, *31*(1), 81-93. https://doi.org/10.1016/j.iac.2010.09.010

Graziano, M. S. (2014). Speculations on the evolution of awareness. *Journal of Cognitive Neuroscience*, *26*(6), 1300-1304. https://doi.org/10.1162/jocn_a_00623

Griffiths, C. E., & Barker, J. N. (2007). Pathogenesis and clinical features of psoriasis. *The Lancet*, *370*(9583), 263-271. https://doi.org/10.1016/S0140-6736(07)61128-3

Gunnar, M., & Quevedo, K. (2007). The neurobiology of stress and development. *Annual Review of Psychology*, *58*, 145-173. https://doi.org/10.1146/annurev.psych.58.110405.085605

Guo, S., & DiPietro, L. A. (2010). Factors affecting wound healing. *Journal of Dental Research, 89*(3), 219-229. https://doi.org/10.1177/0022034509359125

Gurfein, B. T., Davidenko, O., Premenko-Lanier, M., Milush, J. M., Acree, M., Dallman, M. F., Touma, C., Palme, R., York, V. A., Fromentin, G., Darcel, N., Nixon, D. F., & Hecht, F. M. (2014). Environmental enrichment alters splenic immune cell composition and enhances secondary influenza vaccine responses in mice. *Molecular Medicine, 20*(1), 179-190. https://doi.org/10.2119/molmed.2013.00158

Hajek, A., Brettschneider, C., Mallon, T., Ernst, A., Mamone, S., Wiese, B., Weyerer, S., Werle, J., Pentzek, M., Fuchs, A., Stein, J., Luck, T., Bickel, H., Weeg, D., Wagner, M., Heser, K., Maier, W., Scherer, M., Riedel-Heller, S. G., & König, H. (2017). The impact of social engagement on health-related quality of life and depressive symptoms in old age-evidence from a multicenter prospective cohort study in Germany. *Health and Quality of Life Outcomes*, *15*(1), 1-8. https://doi.org/10.1186/s12955-017-0715-8

Hartig, T., van den Berg, A. E., Hagerhall, C. M., Tomalak, M., Bauer, N., Hansmann, R., Ojala, A., Syngollitou, E., Carrus, G., van Herzele, A., Bell, S., Podesta, M. T. C., & Waaseth, W. (2011). Health benefits of nature experience: Psychological, social and cultural processes. In K. Nilsson, M. Sangster, C. Gallis, T. Hartig, S. Vries, K. Seeland, & J. Schipperjin (Eds.) *Forests, Trees and Human Health* (pp. 127-168). Springer. https://doi.org/10.1007/978-90-481-9806-1_5

Hathorn, K., & Nanda, U. (2008). A guide to evidence-based art. *The Center for Health Design*, 1-22.

Hathorn, K., & Ulrich, R. (2001). The therapeutic art program of Northwestern Memorial Hospital. *Creating Environments that Heal: Proceedings of the Symposium on Healthcare Design*.

Hayes, A. F. (2017). *Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach.* Guilford Publications.

Hebb, D. O. (1947). The effects of early experience on problem-solving at maturity. *American Psychologist, 2*, 306-307.

Heerwagen, J. H. (1990). Windows, windowlessness and simulated view. Paper presented at the *Environmental Design Research Association Symposium,* 269-280.

Heller, M. M., Lee, E. S., & Koo, J. Y. (2011). Stress as an influencing factor in psoriasis. *Skin Therapy Letter*, *16*(5), 1-4. https://www.skintherapyletter.com/psoriasis/stress/

Hernández, B., Coïc, Y. M., Pflüger, F., Kruglik, S. G., & Ghomi, M. (2016). All characteristic Raman markers of tyrosine and tyrosinate originate from phenol ring

fundamental vibrations. *Journal of Raman Spectroscopy*, *47*(2), 210-220. https://doi.org/10.1002/jrs.4776

Ho, R. T., Potash, J. S., Fang, F., & Rollins, J. (2015). Art viewing directives in hospital settings effect on mood. *HERD: Health Environments Research & Design Journal*, *8*(3), 30-43. https://doi.org/10.1177/1937586715575903

Hole, J., Hirsch, M., Ball, E., & Meads, C. (2015). Music as an aid for postoperative recovery in adults: A systematic review and meta-analysis. *The Lancet*, *386*(10004), 1659-1671. https://doi.org/10.1016/S0140-6736(15)60169-6

Huang, Z., McWilliams, A., Lui, H., McLean, D. I., Lam, S., & Zeng, H. (2003). Near-infrared Raman spectroscopy for optical diagnosis of lung cancer. *International Journal of Cancer*, *107*(6), 1047-1052. https://doi.org/10.1002/ijc.11500

Hunter, M. R., Gillespie, B. W., & Chen, S. Y. (2019). Urban nature experiences reduce stress in the context of daily life based on salivary biomarkers. *Frontiers in Psychology*, *10*, 722. https://doi.org/10.3389/fpsyg.2019.00722

Ignacio, G., El-Amin, I., & Mendenhall, V. (2016). Animal models for wound healing. In M. Albanna, & J. H. Holmes (Eds.) *Skin Tissue Engineering and Regenerative Medicine* (pp. 387-400). Academic Press/Elsevier.

Inoue, K., Nakamura, M., Sakuma, N., & Okada, M. (2013) Turning off or turning on?: Two different ways to use a baby seal shaped robot paro in occupational therapy for patients with dementia. *Assistive Technology Research Series. 33*, 875-879. https://doi.org/10.3233/978-1-61499-304-9-875

İşeri, S. Ö., Düşünceli, F., Erzik, C., Uslu, B., Arbak, S., & Yeğen, B. Ç. (2010). Oxytocin or social housing alleviates local burn injury in rats. *Journal of Surgical Research, 162*(1), 122-131. https://doi.org/10.1016/j.jss.2009.02.018

IsHak, W. W., Kahloon, M., & Fakhry, H. (2011). Oxytocin role in enhancing well-being: A literature review. *Journal of Affective Disorders*, *130*(1-2), 1-9. https://doi.org/10.1016/j.jad.2010.06.001

Jakob, A., & Collier, L. (2017). Sensory enrichment for people living with dementia: Increasing the benefits of multisensory environments in dementia care through design. *Design for Health*, *1*(1), 115-133. https://doi.org/10.1080/24735132.2017.1296274

Janssen, H., Ada, L., Karayanidis, F., Drysdale, K., McElduff, P., Pollack, M., White, J., Nilsson, M., Bernhardt, J., & Spratt, N. J. (2012). Translating the use of an enriched environment poststroke from bench to bedside: Study design and protocol used to test the feasibility of environmental enrichment on stroke patients in rehabilitation. *International Journal of Stroke, 7*(6), 521-526. https://doi.org/10.1111/j.1747-4949.2011.00727.x

Janssen, H., Ada, L., Bernhardt, J., McElduff, P., Pollack, M., Nilsson, M., & Spratt, N. J. (2014). An enriched environment increases activity in stroke patients undergoing

rehabilitation in a mixed rehabilitation unit: A pilot non-randomized controlled trial. *Disability and Rehabilitation, 36*(3), 255-262. https://doi.org/10.3109/09638288.2013.788218

Janssen, H., Bernhardt, J., Collier, J. M., Sena, E. S., McElduff, P., Attia, J., Pollack, M., Howells, D. W., Nilsson, M., Calford, M. B., & Spratt, N. J. (2010). An enriched environment improves sensorimotor function post-ischemic stroke. *Neurorehabilitation and Neural Repair*, *24*(9), 802-813. https://doi.org/10.1177/1545968310372092

Jo, H., Song, C., & Miyazaki, Y. (2019). Physiological benefits of viewing nature: A systematic review of indoor experiments. *International Journal of Environmental Research and Public Health, 16*(23), 4739. https://doi.org/10.3390/ijerph16234739

Johnson, S. L., & Roberts, J. E. (1995). Life events and bipolar disorder: Implications from biological theories. *Psychological Bulletin*, *117*(3), 434. https://doi.org/10.1037/0033-2909.117.3.434

Joshi, S., Li, Y., Kalwani, R. M., & Gold, J. I. (2016). Relationships between pupil diameter and neuronal activity in the locus coeruleus, colliculi, and cingulate cortex. *Neuron, 89*(1), 221-234. https://doi.org/10.1016/j.neuron.2015.11.028

Jurgens, H. A., & Johnson, R. W. (2012). Environmental enrichment attenuates hippocampal neuroinflammation and improves cognitive function during influenza infection. *Brain, Behavior, and Immunity*, *26*(6), 1006-1016. https://doi.org/10.1016/j.bbi.2012.05.015

Kabat-Zinn, J., Wheeler, E., Light, T., Skillings, A., Scharf, M. J., Cropley, T. G., Thomas, G., Hosmer, D., & Bernhard, J. D. (1998). Influence of a mindfulness meditation-based stress reduction intervention on rates of skin clearing in patients with moderate to severe psoriasis undergoing photo therapy (UVB) and photochemotherapy (PUVA). *Psychosomatic Medicine*, *60*(5), 625-632. https://journals.lww.com/psychosomaticmedicine/Fulltext/1998/09000/Influence_of_a_Mindfulness_Meditation_Based_Stress.20.aspx

Kang, H. S., Makimoto, K., Konno, R., & Koh, I. S. (2019). Review of outcome measures in PARO robot intervention studies for dementia care. *Geriatric Nursing*. *41*(3), 207-214. https://doi.org/10.1016/j.gerinurse.2019.09.003

Kaplan, S., Talbot, J. F., & Kaplan, R. (1988). Coping with daily hassles: The impact of nearby nature on the work environment. *Project Report. USDA Forest Service, North Central Forest Experimental Station, Urban Forestry Unit Cooperative Agreement*, 23-85-08.

Kaplan, S. (1995). The restorative benefits of nature: Toward an integrative framework. *Journal of Environmental Psychology*, *15*(3), 169-182. http://doi.org/10.1016/0272-4944(95)90001-2

Karnik, M., Printz, B., & Finkel, J. (2014). A hospital's contemporary art collection: Effects on patient mood, stress, comfort, and expectations. *HERD: Health Environments Research & Design Journal, 7*(3), 60-77. https://doi.org/10.1177/193758671400700305

Kawaguchi, Y., Wada, K., Okamoto, M., Tsujii, T., Shibata, T., & Sakatani, K. (2012). Investigation of brain activity after interaction with seal robot measured by fNIRS. In *2012 IEEE RO-MAN: The 21st IEEE International Symposium on Robot and Human Interactive Communication* (pp. 571-576). IEEE. http://doi.org/10.1109/ROMAN.2012.6343812

Kelly, P., Williamson, C., Niven, A. G., Hunter, R., Mutrie, N., & Richards, J. (2018). Walking on sunshine: Scoping review of the evidence for walking and mental health. *British Journal of Sports Medicine*, *52*(12), 800-806. http://dx.doi.org/10.1136/bjsports-2017-098827

Kemper, K. J., & Danhauer, S. C. (2005). Music as therapy. *Southern Medical Journal*, *98*(3), 282-288. https://doi.org/10.1097/01.smj.0000154773.11986.39

Khalfa, S., Bella, S. D., Roy, M., Peretz, I., & Lupien, S. J. (2003). Effects of relaxing music on salivary cortisol level after psychological stress. *Annals of the New York Academy of Sciences*, *999*(1), 374-376. https://doi.org/10.1196/annals.1284.045

Khan, F., Amatya, B., Elmalik, A., Lowe, M., Ng, L., Reid, I., & Galea, M. P. (2016). An enriched environmental programme during inpatient neuro-rehabilitation: A randomized controlled trial. *Journal of Rehabilitation Medicine*, *48*(5), 417-425. https://doi.org/10.2340/16501977-2081

Kiecolt-Glaser, J. K., Marucha, P. T., Mercado, A. M., Malarkey, W. B., & Glaser, R. (1995). Slowing of wound healing by psychological stress. *The Lancet*, *346*(8984), 1194-1196. https://doi.org/10.1016/S0140-6736(95)92899-5

King, M. G., Burrows, G. D., & Stanley, G. V. (1983). Measurement of stress and arousal: Validation of the stress/arousal adjective checklist. *British Journal of Psychology*, *74*(4), 473-479. https://doi.org/10.1111/j.2044-8295.1983.tb01880.x

Kirschbaum, C., & Hellhammer, D. H. (2007). Salivary cortisol*. In G. Fink (Ed.), *Encyclopedia of Stress. Vol. 3.* Academic Press.

Kirschbaum, C., Pirke, K. M., & Hellhammer, D. H. (1993). The 'trier social stress test'-- A tool for investigating psychobiological stress responses in a laboratory setting. *Neuropsychobiology*, *28*(1-2), 76-81. https://doi.org/10.1159/000119004

Kirwan, H., & Pignataro, R. (2015). The skin and wound healing. In D. J. Magee, J. E. Zachazewski, W. S. Quillen, & R. C. Manske (Eds.) *Pathology and Intervention in Musculoskeletal Rehabilitation* (pp. 25-62). Elsevier Health Sciences.

Kivimäki, M., & Steptoe, A. (2018). Effects of stress on the development and progression of cardiovascular disease. *Nature Reviews Cardiology*, *15*(4), 215. https://doi.org/10.1038/nrcardio.2017.189

Klein, S. L., Lambert, K. G., Durr, D., Schaefer, T., & Waring, R. E. (1994). Influence of environmental enrichment and sex on predator stress response in rats. *Physiology & Behavior*, *56*(2), 291-297. https://doi.org/10.1016/0031-9384(94)90197-X

Koschwanez, H. E., & Broadbent, E. (2011). The use of wound healing assessment methods in psychological studies: A review and recommendations. *British Journal of Health Psychology, 16*(1), 1-32. https://doi.org/10.1348/135910710X524633

Koschwanez, H. E., Kerse, N., Darragh, M., Jarrett, P., Booth, R. J., & Broadbent, E. (2013). Expressive writing and wound healing in older adults: A randomized controlled trial. *Psychosomatic Medicine, 75*(6), 581-590. http://doi.org/10.1097/PSY.0b013e31829b7b2e

Koschwanez, H., Vurnek, M., Weinman, J., Tarlton, J., Whiting, C., Amirapu, S., Colgan, S., Long, D., Jarrett, P., & Broadbent, E. (2015). Stress-related changes to immune cells in the skin prior to wounding may impair subsequent healing. *Brain, Behavior, and Immunity, 50*, 47-51. https://doi.org/10.1016/j.bbi.2015.06.011

Kotloski, R. J., & Sutula, T. P. (2015). Environmental enrichment: Evidence for an unexpected therapeutic influence. *Experimental Neurology, 264*, 121-126. https://doi.org/10.1016/j.expneurol.2014.11.012

Kotrulja, L., Tadinac, M., JokIć-BegIć, N., & Gregurek, R. (2010). A multivariate analysis of clinical severity, psychological distress and psychopathological traits in psoriatic patients. *Acta Dermato-Venereologica, 90*(3), 251-256. https://doi.org/10.2340/00015555-0838

Krauss, L., Ott, C., Opwis, K., Meyer, A., & Gaab, J. (2019). Impact of contextualizing information on aesthetic experience and psychophysiological responses to art in a museum: A naturalistic randomized controlled trial. *Psychology of Aesthetics, Creativity, and the Arts.* Advance Online Publication. https://doi.org/10.1037/aca0000280

Kweon, B., Ulrich, R. S., Walker, V., & Tassinary, L. (2008). Anger and stress: The role of landscape posters in an office setting. *Environment and Behavior, 40*(3), 355-381. https://doi.org/10.1177/0013916506298797

Lacey, S., Hagtvedt, H., Patrick, V. M., Anderson, A., Stilla, R., Deshpande, G., Hu, X., Sato, J. R., Reddy, S., & Sathian, K. (2011). Art for reward's sake: Visual art recruits the ventral striatum. *Neuroimage, 55*(1), 420-433. https://doi.org/10.1016/j.neuroimage.2010.11.027

Laeng, B., Sirois, S., & Gredebäck, G. (2012). Pupillometry: A window to the preconscious? *Perspectives on Psychological Science, 7*(1), 18-27. https://doi.org/10.1177/1745691611427305

Lankston, L., Cusack, P., Fremantle, C., & Isles, C. (2010). Visual art in hospitals: Case studies and review of the evidence. *Journal of the Royal Society of Medicine, 103*(12), 490-499. https://doi.org/10.1258/jrsm.2010.100256

Lavda, A. C., Webb, T. L., & Thompson, A. R. (2012). A meta-analysis of the effectiveness of psychological interventions for adults with skin conditions. *British Journal of Dermatology, 167*(5), 970-979. https://doi.org/10.1111/j.1365-2133.2012.11183.x

Laviola, G., Rea, M., Morley-Fletcher, S., Di Carlo, S., Bacosi, A., De Simone, R., Bertini, M., & Pacifici, R. (2004). Beneficial effects of enriched environment on adolescent rats from stressed pregnancies. *European Journal of Neuroscience*, *20*(6), 1655-1664. https://doi.org/10.1111/j.1460-9568.2004.03597.x

Law, M., Jarrett, P., Nater, U. M., Skoluda, N., & Broadbent, E. (2020a). The effects of environmental enrichment on skin barrier recovery in humans: A randomised trial. *Scientific Reports*, *10*(1), 1-11. https://doi.org/10.1038/s41598-020-66687-2

Law, M., Jarrett, P., Nater, U. M., Skoluda, N., & Broadbent, E. (2020b). The effects of sensory enrichment after a laboratory stressor on human skin barrier recovery in a randomized trial. *Psychosomatic Medicine*. https://doi.org/10.1097/psy.0000000000000858

Law, M., Minissale, G., Lambert, A., Nater, U. M., Skoluda, N., Ryckman, N., Tahara-Eckl, L., Bandzo, M., & Broadbent, E. (2020). Viewing landscapes is more stimulating than scrambled images after a stressor: A cross-disciplinary approach. *Frontiers in Psychology*, *10*, 3092. https://doi.org/10.3389/fpsyg.2019.03092

Lazarus, R. S., & Folkman, S. (1984). *Stress, Appraisal, and Coping*. Springer.

Leardi, S., Pietroletti, R., Angeloni, G., Necozione, S., Ranalletta, G., & Del Gusto, B. (2007). Randomized clinical trial examining the effect of music therapy in stress response to day surgery. *British Journal of Surgery*, *94*(8), 943-947. https://doi.org/10.1002/bjs.5914

Leroy, M., Lefèvre, T., Pouliot, R., Auger, M., & Laroche, G. (2015). Using infrared and raman microspectroscopies to compare ex vivo involved psoriatic skin with normal human skin. *Journal of Biomedical Optics*, *20*(6), 067004. https://doi.org/10.1117/1.JBO.20.6.067004

Li, S., Chen, G., Zhang, Y., Guo, Z., Liu, Z., Xu, J., Li, X., & Lin, L. (2014). Identification and characterization of colorectal cancer using Raman spectroscopy and feature selection techniques. *Optics Express*, *22*(21), 25895-25908. https://doi.org/10.1364/OE.22.025895

Lu, Y., Liu, M., Shi, S., Jiang, H., Yang, L., Liu, X., Zhang, Q., & Pan, F. (2010). Effects of stress in early life on immune functions in rats with asthma and the effects of music therapy. *Journal of Asthma*, *47*(5), 526-531. https://doi.org/10.3109/02770901003801964

Maarouf, M., Maarouf, C. L., Yosipovitch, G., & Shi, V. Y. (2019). The impact of stress on epidermal barrier function: An evidence-based review. *British Journal of Dermatology*, *181*(6), 1129-1137. https://doi.org/10.1111/bjd.17605

Mackay, C., Cox, T., Burrows, G., & Lazzerini, T. (1978). An inventory for the measurement of self-reported stress and arousal. *British Journal of Social & Clinical Psychology*, *17*(3), 283-284. https://doi.org/10.1111/j.2044-8260.1978.tb00280.x

Mackes, N. K., Golm, D., Sarkar, S., Kumsta, R., Rutter, M., Fairchild, G., Mehta, M. A., & Sonuga-Barke, E. J. (2020). Early childhood deprivation is associated with alterations in

adult brain structure despite subsequent environmental enrichment. *Proceedings of the National Academy of Sciences*, *117*(1), 641-649. https://doi.org/10.1073/pnas.1911264116

Maddock, A., Hevey, D., D'Alton, P., & Kirby, B. (2019). A randomized trial of mindfulness-based cognitive therapy with psoriasis patients. *Mindfulness*, *10*(12), 2606-2619. https://doi.org/10.1007/s12671-019-01242-3

Mastandrea S. (2019) Visitor's approaches, personality traits and psycho-physiological well-being in different art style museums. In A. Luigini (Ed.*) Proceedings of the 1st International and Interdisciplinary Conference on Digital Environments for Education, Arts and Heritage. EARTH 2018. Advances in Intelligent Systems and Computing, vol 919* (pp. 27-33). Springer. https://doi.org/10.1007/978-3-030-12240-9_4

Mastandrea, S., Maricchiolo, F., Carrus, G., Giovannelli, I., Giuliani, V., & Berardi, D. (2019). Visits to figurative art museums may lower blood pressure and stress. *Arts & Health*, *11*(2), 123-132. https://doi.org/10.1080/17533015.2018.1443953

Mazarakis, N. K., Mo, C., Renoir, T., Van Dellen, A., Deacon, R., Blakemore, C., & Hannan, A. J. (2014). 'Super-enrichment' reveals dose-dependent therapeutic effects of environmental stimulation in a transgenic mouse model of Huntington's disease. *Journal of Huntington's Disease*, *3*(3), 299-309. https://doi.org/10.3233/JHD-140118

McCabe, C., Roche, D., Hegarty, F., & McCann, S. (2013). 'Open Window': A randomized trial of the effect of new media art using a virtual window on quality of life in patients' experiencing stem cell transplantation. *Psycho-Oncology*, *22*(2), 330-337. https://doi.org/10.1002/pon.2093

McCullough, M. E., Churchland, P. S., & Mendez, A. J. (2013). Problems with measuring peripheral oxytocin: Can the data on oxytocin and human behavior be trusted? *Neuroscience & Biobehavioral Reviews*, *37*(8), 1485-1492. https://doi.org/10.1016/j.neubiorev.2013.04.018

McDonald, M. W., Hayward, K. S., Rosbergen, I., Jeffers, M. S., & Corbett, D. (2018). Is environmental enrichment ready for clinical application in human post-stroke rehabilitation? *Frontiers in Behavioral Neuroscience*, *12*, 135. https://doi.org/10.3389/fnbeh.2018.00135

McEwen, B. S. (2008). Central effects of stress hormones in health and disease: Understanding the protective and damaging effects of stress and stress mediators. *European Journal of Pharmacology*, *583*(2-3), 174-185. https://doi.org/10.1016/j.ejphar.2007.11.071

McGlynn, S. A., Geiskkovitch, D., Mitzner, T. L., & Rogers, W. A. (2016). PARO's stress-reduction potential for older adults. *Proceedings of the Human Factors and Ergonomics Society Annual Meeting*, *60*(1), 1799-1803. https://doi.org/10.1177/1541931213601411

McLaughlin, K. A., Sheridan, M. A., Tibu, F., Fox, N. A., Zeanah, C. H., & Nelson, C. A. (2015). Causal effects of the early caregiving environment on development of stress

response systems in children. *Proceedings of the National Academy of Sciences*, *112*(18), 5637-5642. https://doi.org/10.1073/pnas.1423363112

Meesters, A., den Bosch-Meevissen, Y. M. I., Weijzen, C. A., Buurman, W. A., Losen, M., Schepers, J., Thissen, M. R. T. M., Alberts, H. J. E. M., Schalkwijk, C. G., & Peters, M. L. (2018). The effect of Mindfulness-Based Stress Reduction on wound healing: A preliminary study. *Journal of Behavioral Medicine, 41*(3), 385-397. https://doi.org/10.1007/s10865-017-9901-8

Mesa-Gresa, P., Ramos-Campos, M., & Redolat, R. (2016). Corticosterone levels and behavioral changes induced by simultaneous exposure to chronic social stress and enriched environments in NMRI male mice. *Physiology & Behavior, 158*, 6-17. https://doi.org/10.1016/j.physbeh.2016.02.027

Miller, G. E., & Cohen, S. (2001). Psychological interventions and the immune system: A meta-analytic review and critique. *Health Psychology, 20*(1), 47. https://doi.org/10.1037/0278-6133.20.1.47

Miller, R., & Kirschbaum, C. (2013). Trier social stress test. In M. D. Gellman, & J. R. Turner (Eds.) *Encyclopedia of Behavioral Medicine* (pp. 2005-2008). Springer. https://doi.org/10.1007/978-1-4419-1005-9

Moghaddasifar, I., Fereidooni-Moghadam, M., Fakharzadeh, L., & Haghighi-Zadeh, M. H. (2019). Investigating the effect of multisensory stimulation on depression and anxiety of the elderly nursing home residents: A randomized controlled trial. *Perspectives in Psychiatric Care, 55*(1), 42-47. https://doi.org/10.1111/ppc.12285

Moncek, F., Duncko, R., Johansson, B. B., & Jezova, D. (2004). Effect of environmental enrichment on stress related systems in rats. *Journal of Neuroendocrinology, 16*(5), 423-431. https://doi.org/10.1111/j.1365-2826.2004.01173.x

Moon, H. S., Mizara, A., & McBride, S. R. (2013). Psoriasis and psycho-dermatology. *Dermatology and Therapy*, *3*(2), 117-130. https://doi.org/10.1007/s13555-013-0031-0

Morhenn, V. B., Nelson, T. E., & Gruol, D. L. (2013). The rate of wound healing is increased in psoriasis. *Journal of Dermatological Science, 72*(2), 87-92. https://doi.org/10.1016/j.jdermsci.2013.06.001

Morley-Fletcher, S., Rea, M., Maccari, S., & Laviola, G. (2003). Environmental enrichment during adolescence reverses the effects of prenatal stress on play behaviour and HPA axis reactivity in rats. *European Journal of Neuroscience, 18*(12), 3367-3374. https://doi.org/10.1111/j.1460-9568.2003.03070.x

Morris, M. C., Ciesla, J. A., & Garber, J. (2010). A prospective study of stress autonomy versus stress sensitization in adolescents at varied risk for depression. *Journal of Abnormal Psychology*, *119*(2), 341. http://doi.org/10.1037/a0019036

Muizzuddin, N., Matsui, M. S., Marenus, K. D., & Maes, D. H. (2003). Impact of stress of marital dissolution on skin barrier recovery: Tape stripping and measurement of trans-

epidermal water loss (TEWL). *Skin Research and Technology*, *9*(1), 34-38. https://doi.org/10.1034/j.1600-0846.2003.00354.x

Nachat-Kappes, R., Pinel, A., Combe, K., Lamas, B., Farges, M., Rossary, A., Goncalves-Mendes, N., Caldefie-Chezet, F., Vasson, M., & Basu, S. (2012). Effects of enriched environment on COX-2, leptin and eicosanoids in a mouse model of breast cancer. *PLoS One*, *7*(12), e51525. https://doi.org/10.1371/journal.pone.0051525

Nair, S., Sagar, M., Sollers, J., Consedine, N., & Broadbent, E. (2015). Do slumped and upright postures affect stress responses? A randomized trial. *Health Psychology*, *34*(6), 632-641. https://doi.org/10.1037/hea0000146

Nanda, U., Barbato Gaydos, H. L., Hathorn, K., & Watkins, N. (2010). Art and posttraumatic stress: A review of the empirical literature on the therapeutic implications of artwork for war veterans with posttraumatic stress disorder. *Environment and Behavior*, *42*(3), 376-390. https://doi.org/10.1177/0013916510361874

Nanda, U., Eisen, S. L., & Baladandayuthapani, V. (2008). Undertaking an art survey to compare patient versus student art preferences. *Environment and Behavior*, *40*(2), 269-301. https://doi.org/10.1177/0013916507311552

Nanda, U., Eisen, S. L., Zadeh, R. S., & Owen, D. (2011). Effect of visual art on patient anxiety and agitation in a mental health facility and implications for the business case. *Journal of Psychiatric and Mental Health Nursing*, *18*(5), 386-393. https://doi.org/10.1111/j.1365-2850.2010.01682.x

Nawaz, A., Batool, Z., Ahmed, S., Khaliq, S., Sajid, I., Anis, L., & Haider, S. (2017). Attenuation of restraint stress-induced behavioral deficits by environmental enrichment in male rats. *Pakistan Veterinary Journal*, *37*(4), 435-439. http://www.pvj.com.pk/

Neerackal, R. J., Abdul Latheef, E. N., Sukumarakurup, S., & Jafferany, M. (2020). Relaxation therapy in the management of psoriasis. *Dermatologic Therapy*, e14030. https://doi.org/10.1111/dth.14030

Nomura, T., & Hoshina, Y. (2017). How different types of animal robots differently influence elder and younger people's mental states? In *Proceedings of the Companion of the 2017 ACM/IEEE International Conference on Human-Robot Interaction* (pp. 231-232). Association for Computing Machinery. https://doi.org/10.1145/3029798.3038405

Normann, M. C., McNeal, N., Dagner, A., Ihm, E., Woodbury, M., & Grippo, A. J. (2018). The influence of environmental enrichment on cardiovascular and behavioral responses to social stress. *Psychosomatic Medicine*, *80*(3), 271-277. https://doi.org/10.1097/PSY.0000000000000558

Novaes, L. S., dos Santos, N. B., Batalhote, R. F. P., Malta, M. B., Camarini, R., Scavone, C., & Munhoz, C. D. (2017). Environmental enrichment protects against stress-induced anxiety: Role of glucocorticoid receptor, ERK, and CREB signaling in the basolateral amygdala. *Neuropharmacology*, *113*, 457-466. https://doi.org/10.1016/j.neuropharm.2016.10.026

O'Connor, D. B., Thayer, J. F., & Vedhara, K. (2020). Stress and health: A review of psychobiological processes. *Annual Review of Psychology*, *72*. https://doi.org/10.1146/annurev-psych-062520-122331

O'Leary, C. J., Creamer, D., Higgins, E., & Weinman, J. (2004). Perceived stress, stress attributions and psychological distress in psoriasis. *Journal of Psychosomatic Research*, *57*(5), 465-471. https://doi.org/10.1016/j.jpsychores.2004.03.012

Olafsdottir, G., Cloke, P., Schulz, A., Van Dyck, Z., Eysteinsson, T., Thorleifsdottir, B., & Vögele, C. (2020). Health benefits of walking in nature: A randomized controlled study under conditions of real-life stress. *Environment and Behavior*, *52*(3), 248-274. https://doi.org/10.1177/0013916518800798

Ouyang, H., Xu, J., Zhu, Z., Long, T., & Yu, C. (2015). Rapid discrimination of malignant lesions from normal gastric tissues utilizing Raman spectroscopy system: A meta-analysis. *Journal of Cancer Research and Clinical Oncology*, *141*(10), 1835-1844. https://doi.org/10.1007/s00432-015-1971-9

Padgett, D. A., & Glaser, R. (2003). How stress influences the immune response. *Trends in Immunology*, *24*(8), 444-448. https://doi.org/10.1016/S1471-4906(03)00173-X

Paradisi, A., Abeni, D., Finore, E., Di Pietro, C., Sampogna, F., Mazzanti, C., Pilla, M. A., & Tabolli, S. (2010). Effect of written emotional disclosure interventions in persons with psoriasis undergoing narrow band ultraviolet B phototherapy. *European Journal of Dermatology*, *20*(5), 599-605. https://doi.org/10.1684/ejd.2010.1018

Parker, F. S. (1983). *Applications of infrared, Raman, and resonance Raman spectroscopy in biochemistry*. Springer Science & Business Media.

Pearson, M., Gaines, K., Pati, D., Colwell, M., Motheral, L., & Adams, N. G. (2019). The physiological impact of window murals on pediatric patients. *HERD: Health Environments Research & Design Journal*, *12*(2), 116-129. https://doi.org/10.1177/1937586718800483

Peters, M. D. J., Godfrey, C., McInerney, P., Munn, Z., Tricco, A. C., & Khalil, H. (2020). Chapter 11: Scoping reviews (2020 version). In E. Aromataris & Z. Munn Z (Eds.) *Joanna Briggs Institute Reviewer's Manual*, JBI. https://doi.org/10.46658/JBIMES-20-12

Petersen, S. E., & Posner, M. I. (2012). The attention system of the human brain: 20 years after. *Annual Review of Neuroscience, 35*, 73-89. https://doi.org/10.1146/annurev-neuro-062111-150525

Petrie, K. J., Faasse, K., Crichton, F., & Grey, A. (2014). How common are symptoms? Evidence from a New Zealand national telephone survey. *BMJ Open*, *4*(6), e005374. http://dx.doi.org/10.1136/bmjopen-2014-005374

Pham, T. M., Hagman, B., Codita, A., Van Loo, P. L. P., Strömmer, L., & Baumans, V. (2010). Housing environment influences the need for pain relief during post-operative

recovery in mice. *Physiology & Behavior*, *99*(5), 663-668. https://doi.org/10.1016/j.physbeh.2010.01.038

Piaserico, S., Marinello, E., Dessi, A., Linder, M. D., Coccarielli, D., & Peserico, A. (2016). Efficacy of biofeedback and cognitive-behavioural therapy in psoriatic patients: A single-blind, randomized and controlled study with added narrow-band ultraviolet B therapy. *Acta Dermato-Venereologica*, *96*(217), 91-95. https://doi.org/10.2340/00015555-2428

Portugal-Cohen, M., Horev, L., Ruffer, C., Schlippe, G., Voss, W., Ma'or, Z., Oron, M., Soroka, Y., Frušić-Zlotkin, M., Milner, Y., & Kohen, R. (2012). Non-invasive skin biomarkers quantification of psoriasis and atopic dermatitis: Cytokines, antioxidants and psoriatic skin auto-fluorescence. *Biomedicine & Pharmacotherapy*, *66*(4), 293-299. https://doi.org/10.1016/j.biopha.2011.12.009

Posner, M. I., & Petersen, S. E. (1990). The attention system of the human brain. *Annual Review of Neuroscience, 13*(1), 25-42. https://doi.org/10.1146/annurev.ne.13.030190.000325

Price, M. L., Mottahedin, I., & Mayo, P. R. (1991). Can psychotherapy help patients with psoriasis? *Clinical and Experimental Dermatology, 16*(2), 114-117. https://doi.org/10.1111/j.1365-2230.1991.tb00319.x

Pyter, L. M., Yang, L., da Rocha, J. M., & Engeland, C. G. (2014). The effects of social isolation on wound healing mechanisms in female mice. *Physiology & Behavior*, *127*, 64-70. https://doi.org/10.1016/j.physbeh.2014.01.008

Queen, N. J., Hassan, Q. N., & Cao, L. (2020). Improvements to healthspan through environmental enrichment and lifestyle interventions: Where are we now? *Frontiers in Neuroscience, 14*, 605. https://doi.org/10.3389/fnins.2020.00605

Qureshi, A. A., Awosika, O., Baruffi, F., Rengifo-Pardo, M., & Ehrlich, A. (2019). Psychological therapies in management of psoriatic skin disease: A systematic review. *American Journal of Clinical Dermatology*, *20*, 607-624. https://doi.org/10.1007/s40257-019-00437-7

Radstaak, M., Geurts, S. A. E., Rosschot, J. F. B., & Kompier, M. A. J. (2014). Music and psychophysiological recovery from stress. *Psychosomatic Medicine, 76*(7), 529-537. http://doi.org/10.1097/PSY.0000000000000094

Ragu Varman, D., Marimuthu, G., & Rajan, K. E. (2012). Environmental enrichment exerts anxiolytic effects in the Indian field mouse (Mus booduga). *Applied Animal Behaviour Science*, *136*(2-4), 166-173. https://doi.org/10.1016/j.applanim.2011.12.003

Rajka, G., & Thune, P. (1976). The relationship between the course of psoriasis and transepidermal water loss, photoelectric plethysmography and reflex photometry. *British Journal of Dermatology*, *94*(3), 253-261. https://doi.org/10.1111/j.1365-2133.1976.tb04381.x

Randall, N., Bennett, C. C., Šabanović, S., Nagata, S., Eldridge, L., Collins, S., & Piatt, J. A. (2019). More than just friends: In-home use and design recommendations for sensing socially assistive robots (SARs) by older adults with depression. *Paladyn, Journal of Behavioral Robotics*, *10*(1), 237-255. https://doi.org/10.1515/pjbr-2019-0020

Rasmussen, H. N., Scheier, M. F., & Greenhouse, J. B. (2009). Optimism and physical health: A meta-analytic review. *Annals of Behavioral Medicine*, *37*(3), 239-256. https://doi.org/10.1007/s12160-009-9111-x

Raychaudhuri, S. P., Jiang, W., & Raychaudhuri, S. K. (2008). Revisiting the koebner phenomenon: Role of NGF and its receptor system in the pathogenesis of psoriasis. *The American Journal of Pathology*, *172*(4), 961-971. https://doi.org/10.2353/ajpath.2008.070710

Reid, B. M., Coe, C. L., Doyle, C. M., Sheerar, D., Slukvina, A., Donzella, B., & Gunnar, M. R. (2019). Persistent skewing of the T-cell profile in adolescents adopted internationally from institutional care. *Brain, Behavior, and Immunity*, *77*, 168-177. https://doi.org/10.1016/j.bbi.2019.01.001

Reinke, J. M., & Sorg, H. (2012). Wound repair and regeneration. *European Surgical Research*, *49*(1), 35-43. https://doi.org/10.1159/000339613

Renton, A., Phillips, G., Daykin, N., Yu, G., Taylor, K., & Petticrew, M. (2012). Think of your art-eries: Arts participation, behavioural cardiovascular risk factors and mental well-being in deprived communities in London. *Public Health*, *126*, S57-S64. https://doi.org/10.1016/j.puhe.2012.05.025

Repetto, C., Serino, S., Macedonia, M., & Riva, G. (2016). Virtual reality as an embodied tool to enhance episodic memory in elderly. *Frontiers in Psychology*, *7*, 1839. https://doi.org/10.3389/fpsyg.2016.01839

Reynolds, S., Lane, S. J., & Richards, L. (2010). Using animal models of enriched environments to inform research on sensory integration intervention for the rehabilitation of neurodevelopmental disorders. *Journal of Neurodevelopmental Disorders*, *2*(3), 120. http://doi.org/10.1007/s11689-010-9053-4

Robinson, H., Jarrett, P., & Broadbent, E. (2015). The effects of relaxation before or after skin damage on skin barrier recovery: A preliminary study. *Psychosomatic Medicine*, *77*(8), 844-852. http://doi.org/10.1097/PSY.0000000000000222

Robinson, H., Jarrett, P., Vedhara, K., & Broadbent, E. (2017). The effects of expressive writing before or after punch biopsy on wound healing. *Brain, Behavior, and Immunity*, *61*, 217-227. https://doi.org/10.1016/j.bbi.2016.11.025

Robinson, H., MacDonald, B., & Broadbent, E. (2015). Physiological effects of a companion robot on blood pressure of older people in residential care facility: A pilot study. *Australasian Journal on Ageing*, *34*(1), 27-32. https://doi.org/10.1111/ajag.12099

Robinson, H., MacDonald, B., Kerse, N., & Broadbent, E. (2013). The psychosocial effects of a companion robot: A randomized controlled trial. *Journal of the American Medical Directors Association*, *14*(9), 661-667. https://doi.org/10.1016/j.jamda.2013.02.007

Robinson, H., Norton, S., Jarrett, P., & Broadbent, E. (2017). The effects of psychological interventions on wound healing: A systematic review of randomized trials. *British Journal of Health Psychology*, *22*(4), 805-835. https://doi.org/10.1111/bjhp.12257

Robinson, H., Ravikulan, A., Nater, U. M., Skoluda, N., Jarrett, P., & Broadbent, E. (2017). The role of social closeness during tape stripping to facilitate skin barrier recovery: Preliminary findings. *Health Psychology*, *36*(7), 619. https://doi.org/10.1037/hea0000492

Robles, T. F. (2007). Stress, social support, and delayed skin barrier recovery. *Psychosomatic Medicine*, *69*(8), 807-815. http://doi.org/10.1097/PSY.0b013e318157b12e

Robles, T. F., Brooks, K. P., & Pressman, S. D. (2009). Trait positive affect buffers the effects of acute stress on skin barrier recovery. *Health Psychology*, *28*(3), 373. http://doi.org/10.1037/a0014662

Rogiers, V. (2001). EEMCO guidance for the assessment of transepidermal water loss in cosmetic sciences. *Skin Pharmacology and Physiology*, *14*(2), 117-128. https://doi.org/10.1159/000056341

Rojas, I. G., Padgett, D. A., Sheridan, J. F., & Marucha, P. T. (2002). Stress-induced susceptibility to bacterial infection during cutaneous wound healing. *Brain, Behavior, and Immunity*, *16*(1), 74-84. https://doi.org/10.1006/brbi.2000.0619

Rosbergen, I. C., Grimley, R. S., Hayward, K. S., Walker, K. C., Rowley, D., Campbell, A. M., McGufficke, S., Robertson, S. T., Trinder, J., Janssen, H., & Brauer, S. G. (2016). The effect of an enriched environment on activity levels in people with stroke in an acute stroke unit: Protocol for a before-after pilot study. *Pilot and Feasibility Studies*, *2*(1), 1-6. https://doi.org/10.1186/s40814-016-0081-z

Rosbergen, I. C., Grimley, R. S., Hayward, K. S., Walker, K. C., Rowley, D., Campbell, A. M., McGufficke, S., Robertson, S. T., Trinder, J., Janssen, H., & Brauer, S. G. (2017). Embedding an enriched environment in an acute stroke unit increases activity in people with stroke: A controlled before–after pilot study. *Clinical Rehabilitation, 31*(11), 1516-1528. https://doi.org/10.1177/0269215517705181

Ross, C. M. (2017). Facilitating environmental enrichment in senior care activities with professional development. *Walden Dissertations and Doctoral Studies, 3203.* https://scholarworks.waldenu.edu/dissertations/3203

Roth, A. J., Kornblith, A. B., Batel-Copel, L., Peabody, E., Scher, H. I., & Holland, J. C. (1998). Rapid screening for psychologic distress in men with prostate carcinoma: A pilot study. *Cancer*, *82*(10), 1904-1908. http://doi.org/10.1002/(sici)1097-0142(19980515)82:10<1904::aid-cncr13>3.0.co;2-x

Rousset, L., & Halioua, B. (2018). Stress and psoriasis. *International Journal of Dermatology*, *57*(10), 1165-1172. https://doi.org/10.1111/ijd.14032

Šabanović, S., Bennett, C. C., Chang, W. L., & Huber, L. (2013). PARO robot affects diverse interaction modalities in group sensory therapy for older adults with dementia. In *2013 IEEE 13th International Conference on Rehabilitation Robotics (ICORR)* (pp. 1-6). IEEE. http://doi.org/10.1109/ICORR.2013.6650427

Saito, T., Shibata, T., Wada, K., & Tanie, K. (2003). Relationship between interaction with the mental commit robot and change of stress reaction of the elderly. *Proceedings 2003 IEEE International Symposium on Computational Intelligence in Robotics and Automation. Computational Intelligence in Robotics and Automation for the New Millennium, 1*, 119-124. http://doi.org/10.1109/CIRA.2003.1222074.

Sale, A. (2018). A systematic look at environmental modulation and its impact in brain development. *Trends in Neurosciences*, *41*(1), 4-17. https://doi.org/10.1016/j.tins.2017.10.004

Sampedro-Piquero, P., & Begega, A. (2017). Environmental enrichment as a positive behavioral intervention across the lifespan. *Current Neuropharmacology*, *15*(4), 459-470. https://doi.org/10.2174/1570159X14666160325115909

Schapiro, S. J. (2002). Effects of social manipulations and environmental enrichment on behavior and cell-mediated immune responses in rhesus macaques. *Pharmacology Biochemistry and Behavior*, *73*(1), 271-278. https://doi.org/10.1016/S0091-3057(02)00779-7

Schneiderman, N., Ironson, G., & Siegel, S. D. (2005). Stress and health: Psychological, behavioral, and biological determinants. *Annual Review of Clinical Psychology*, *1*, 607-628. https://doi.org/10.1146/annurev.clinpsy.1.102803.144141

Schrijver, N. C., Bahr, N. I., Weiss, I. C., & Würbel, H. (2002). Dissociable effects of isolation rearing and environmental enrichment on exploration, spatial learning and HPA activity in adult rats. *Pharmacology Biochemistry and Behavior*, *73*(1), 209-224. https://doi.org/10.1016/S0091-3057(02)00790-6

Segerstrom, S. C., & Miller, G. E. (2004). Psychological stress and the human immune system: A meta-analytic study of 30 years of inquiry. *Psychological Bulletin*, *130*(4), 601. http://doi.org/10.1037/0033-2909.130.4.601

Seong, H. H., Park, J. M., & Kim, Y. J. (2018). Antidepressive effects of environmental enrichment in chronic stress–induced depression in rats. *Biological Research for Nursing*, *20*(1), 40-48. https://doi.org/10.1177/1099800417730400

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

Shah, R., & Bewley, A. (2014). Psoriasis: 'The badge of shame'. A case report of a psychological intervention to reduce and potentially clear chronic skin disease. *Clinical and Experimental Dermatology*, *39*(5), 600-603. https://doi.org/10.1111/ced.12339

Shibata, T., & Coughlin, J. F. (2014). Trends of robot therapy with neurological therapeutic seal robot, PARO. *Journal of Robotics and Mechatronics*, *26*(4), 418-425. https://doi.org/10.20965/jrm.2014.p0418

Shirai, K., Iso, H., Ohira, T., Ikeda, A., Noda, H., Honjo, K., Inoue, M., & Tsugane, S. (2009). Perceived level of life enjoyment and risks of cardiovascular disease incidence and mortality. *Circulation*, *120*(11), 956-963. http://doi.org/10.1161/circulationaha.108.834176

Sijercic, I., Ennis, N., & Monson, C. M. (2020). A systematic review of cognitive and behavioral treatments for individuals with psoriasis. *Journal of Dermatological Treatment*, *31*(6), 631-638. https://doi.org/10.1080/09546634.2019.1690625

Singhal, G., Jaehne, E. J., Corrigan, F., & Baune, B. T. (2014). Cellular and molecular mechanisms of immunomodulation in the brain through environmental enrichment. *Frontiers in Cellular Neuroscience*, *8*, 97. https://doi.org/10.3389/fncel.2014.00097

Siri, F., Ferroni, F., Ardizzi, M., Kolesnikova, A., Beccaria, M., Rocci, B., Christov-Bakargiev, C., & Gallese, V. (2018). Behavioral and autonomic responses to real and digital reproductions of works of art. *Progress in Brain Research*, *237*, 201-221. https://doi.org/10.1016/bs.pbr.2018.03.020

Sirois, S., & Brisson, J. (2014). Pupillometry. *Wiley Interdisciplinary Reviews: Cognitive Science*, *5*(6), 679-692. https://doi.org/10.1002/wcs.1323

Skoluda, N., Strahler, J., Schlotz, W., Niederberger, L., Marques, S., Fischer, S., Thoma, M. V., Spoerri, C., Ehlert, U., & Nater, U. M. (2015). Intra-individual psychological and physiological responses to acute laboratory stressors of different intensity. *Psychoneuroendocrinology*, *51*, 227-236. https://doi.org/10.1016/j.psyneuen.2014.10.002

Snast, I., Reiter, O., Atzmony, L., Leshem, Y. A., Hodak, E., Mimouni, D., & Pavlovsky, L. (2018). Psychological stress and psoriasis: A systematic review and meta-analysis. *British Journal of Dermatology*, *178*(5), 1044-1055. https://doi.org/10.1111/bjd.16116

Spitzer, R. L., Kroenke, K., & Williams, J. B. (1999). Patient health questionnaire primary care study group: Validation and utility of a self-report version of prime-md: The PHQ primary care study. *JAMA*, *282*(18), 1737-1744. https://doi.org/10.1001/jama.282.18.1737

Staricoff, R., Loppert, S., Kirklin, D., & Richardson, R. (2003). Integrating the arts into health care: Can we affect clinical outcomes. In D. Kirklan & R. Richardson (Eds.) *The Healing Environment: Without and Within* (pp. 63-80). Royal College of Physicians.

Steptoe, A., Wardle, J., & Marmot, M. (2005). Positive affect and health-related neuroendocrine, cardiovascular, and inflammatory processes. *Proceedings of the*

National Academy of Sciences, *102*(18), 6508-6512. https://doi.org/10.1073/pnas.0409174102

Stewart, T. J., Tong, W., & Whitfeld, M. J. (2018). The associations between psychological stress and psoriasis: A systematic review. *International Journal of Dermatology*, *57*(11), 1275-1282. https://doi.org/10.1111/ijd.13956

Stone, N., Stavroulaki, P., Kendall, C., Birchall, M., & Barr, H. (2000). Raman spectroscopy for early detection of laryngeal malignancy: Preliminary results. *The Laryngoscope*, *110*(10), 1756-1763. https://doi.org/10.1097/00005537-200010000-00037

Strahler, J., Doerr, J. M., Ditzen, B., Linnemann, A., Skoluda, N., & Nater, U. M. (2016). Physical activity buffers fatigue only under low chronic stress. *Stress*, *19*(5), 535-541. https://doi.org/10.1080/10253890.2016.1192121

Strahler, J., Skoluda, N., Kappert, M. B., & Nater, U. M. (2017). Simultaneous measurement of salivary cortisol and alpha-amylase: Application and recommendations. *Neuroscience & Biobehavioral Reviews*, *83*, 657-677. https://doi.org/10.1016/j.neubiorev.2017.08.015

Strøm, B. S., Ytrehus, S., & Grov, E. K. (2016). Sensory stimulation for persons with dementia: A review of the literature. *Journal of Clinical Nursing*, *25*(13-14), 1805-1834. https://doi.org/10.1111/jocn.13169

Suter, E., & Baylin, D. (2007). Choosing art as a complement to healing. *Applied Nursing Research*, *20*(1), 32-38. https://doi.org/10.1016/j.apnr.2005.11.004

Talari, A. C. S., Movasaghi, Z., Rehman, S., & Rehman, I. U. (2015). Raman spectroscopy of biological tissues. *Applied Spectroscopy Reviews*, *50*(1), 46-111. https://doi.org/10.1080/05704928.2014.923902

Tausk, F., & Whitmore, S. E. (1999). A pilot study of hypnosis in the treatment of patients with psoriasis. *Psychotherapy and Psychosomatics*, *68*(4), 221-225. https://doi.org/10.1159/000012336

Thayer, J. F., Hansen, A. L., Saus-Rose, E., & Johnsen, B. H. (2009). Heart rate variability, prefrontal neural function, and cognitive performance: The neurovisceral integration perspective on self-regulation, adaptation, and health. *Annals of Behavioral Medicine*, *37*(2), 141-153. https://doi.org/10.1007/s12160-009-9101-z

Thoma, M. V., Zemp, M., Kreienbühl, L., Hofer, D., Schmidlin, P. R., Attin, T., Ehlert, U., & Nater, U. M. (2015). Effects of music listening on pre-treatment anxiety and stress levels in a dental hygiene recall population. *International Journal of Behavioral Medicine*, *22*(4), 498-505. https://doi.org/10.1007/s12529-014-9439-x

Tops, M., Boksem, M. A., Wester, A. E., Lorist, M. M., & Meijman, T. F. (2006). Task engagement and the relationships between the error-related negativity, agreeableness, behavioral shame proneness and cortisol. *Psychoneuroendocrinology*, *31*(7), 847-858. https://doi.org/10.1016/j.psyneuen.2006.04.001

Tortora, G. J., & Derrickson, B. H. (2018). *Principles of Anatomy and Physiology*. John Wiley & Sons.

Tsai, J. C., Feingold, K. R., Crumrine, D., Wood, L. C., Grunfeld, C., & Elias, P. M. (1994). Permeability barrier disruption alters the localization and expression of TNFα/protein in the epidermis. *Archives of Dermatological Research, 286*(5), 242-248. https://doi.org/10.1007/BF00387595

Tsai, J. L., Knutson, B., & Fung, H. H. (2006). Cultural variation in affect valuation. *Journal of Personality and Social Psychology*, *90*(2), 288. https://doi.org/10.1037/0022-3514.90.2.288

Tschacher, W., Greenwood, S., Kirchberg, V., Wintzerith, S., van den Berg, K., & Tröndle, M. (2012). Physiological correlates of aesthetic perception of artworks in a museum. *Psychology of Aesthetics, Creativity, and the Arts*, *6*(1), 96. https://doi.org/10.1037/a0023845

Tyack, C., Camic, P. M., Heron, M. J., & Hulbert, S. (2017). Viewing art on a tablet computer: A well-being intervention for people with dementia and their caregivers. *Journal of Applied Gerontology*, *36*(7), 864-894. https://doi.org/10.1177/0733464815617287

Ulrich, R. S. (1979). Visual landscapes and psychological well-being. *Landscape Research, 4*(1), 17-23. https://doi.org/10.1080/01426397908705892

Ulrich, R. S. (1981). Natural versus urban scenes: Some psychophysiological effects. *Environment and Behavior, 13*(5), 523-556. https://doi.org/10.1177/0013916581135001

Ulrich, R. S. (1984). View through a window may influence recovery from surgery. *Science*, *224*(4647), 420-421. https://doi.org/10.1126/science.6143402

Ulrich, R. S. (1992). How design impacts wellness. T*he Healthcare Forum Journal*, *35*(5), 20-25.

Ulrich, R. S., Lundén, O., & Eltinge, J. L. (1993). Effects of exposure to nature and abstract pictures on patients recovering from heart surgery. Paper presented at the *Thirty-Third Meeting of the Society of Psychophysiological Research*, *30*(7).

Ulrich, R. S., Simons, R. F., Losito, B. D., & Fiorito, E. (1991). Stress recovery during exposure to natural and urban environments. *Journal of Environmental Psychology, 11*(3), 201-230. https://doi.org/10.1016/S0272-4944(05)80184-7

Ulrich, R. S., Simons, R., & Miles, M. (2003). Effects of environmental simulations and television on blood donor stress. *Journal of Architectural and Planning Research, 20*(1), 38-47. https://www.jstor.org/stable/43030641

Ulrich, R. S., Zimring, C., Quan, X., & Joseph, A. (2006). The environment's impact on stress. In S. Marberry (Ed.) *Improving Healthcare with Better Building Design* (pp. 37-61). Health Administration Press/ACHE Management Series.

Uvnäs-Moberg, K., Handlin, L., & Petersson, M. (2015). Self-soothing behaviors with particular reference to oxytocin release induced by non-noxious sensory stimulation. *Frontiers in Psychology, 5*, 1529. https://doi.org/10.3389/fpsyg.2014.01529

Väänänen, A., Murray, M., Koskinen, A., Vahtera, J., Kouvonen, A., & Kivimäki, M. (2009). Engagement in cultural activities and cause-specific mortality: Prospective cohort study. *Preventive Medicine*, *49*(2-3), 142-147. https://doi.org/10.1016/j.ypmed.2009.06.026

Vargas-Obieta, E., Martínez-Espinosa, J. C., Martínez-Zerega, B. E., Jave-Suárez, L. F., Aguilar-Lemarroy, A., & González-Solís, J. L. (2016). Breast cancer detection based on serum sample surface enhanced Raman spectroscopy. *Lasers in Medical Science*, *31*(7), 1317-1324. https://doi.org/10.1007/s10103-016-1976-x

Vartanian, O., & Skov, M. (2014). Neural correlates of viewing paintings: Evidence from a quantitative meta-analysis of functional magnetic resonance imaging data. *Brain and Cognition, 87*, 52-56. https://doi.org/10.1016/j.bandc.2014.03.004

Vasey, M. W., & Thayer, J. F. (1987). The continuing problem of false positives in repeated measures ANOVA in psychophysiology: A multivariate solution. *Psychophysiology, 24*(4), 479-486. https://doi.org/10.1111/j.1469-8986.1987.tb00324.x

Vedhara, K., Morris, R. M., Booth, R., Horgan, M., Lawrence, M., & Birchall, N. (2007). Changes in mood predict disease activity and quality of life in patients with psoriasis following emotional disclosure. *Journal of Psychosomatic Research*, *62*(6), 611-619. https://doi.org/10.1016/j.jpsychores.2006.12.017

Vegas, Ó., VanBuskirk, J., Richardson, S., Parfitt, D., Helmreich, D., Rempel, M., Moynihan, J., & Tausk, F. (2012). Effects of psychological stress and housing conditions on the delay of wound healing. *Psicothema*, *24*(4), 581-586. https://www.redalyc.org/articulo.oa?id=72723959012

Velarde, M. D., Fry, G., & Tveit, M. (2007). Health effects of viewing landscapes–Landscape types in environmental psychology. *Urban Forestry & Urban Greening*, *6*(4), 199-212. https://doi.org/10.1016/j.ufug.2007.07.001

Velnar, T., Bailey, T., & Smrkolj, V. (2009). The wound healing process: An overview of the cellular and molecular mechanisms. *Journal of International Medical Research*, *37*(5), 1528-1542. https://doi.org/10.1177/147323000903700531

Verhoeven, E. W. M., Kraaimaat, F. W., De Jong, E. M. G. J., Schalkwijk, J., Van De Kerkhof, P. C. M., & Evers, A. W. M. (2009). Individual differences in the effect of daily stressors on psoriasis: A prospective study. *British Journal of Dermatology*, *161*(2), 295-299. https://doi.org/10.1111/j.1365-2133.2009.09194.x

Vetter, D., Barth, J., Uyulmaz, S., Uyulmaz, S., Vonlanthen, R., Belli, G., Montorsi, M., Bismuth, H., Witt, C. M., & Clavien, P. (2015). Effects of art on surgical patients: A systematic review and meta-analysis. *Annals of Surgery*, *262*(5), 704-713. https://doi.org/10.1097/SLA.0000000000001480

Vileikyte, L. (2007). Stress and wound healing. *Clinics in Dermatology*, *25*(1), 49-55. https://doi.org/10.1016/j.clindermatol.2006.09.005

Villani, D., & Riva, G. (2012). Does interactive media enhance the management of stress? Suggestions from a controlled study. *Cyberpsychology, Behavior, and Social Networking*, *15*(1), 24-30. https://doi.org/10.1089/cyber.2011.0141

Vitalo, A., Fricchione, J., Casali, M., Berdichevsky, Y., Hoge, E. A., Rauch, S. L., Berthiaume, F., Yarmush, M. L., Benson, H., Fricchione, G. L., & Levine, J. B. (2009). Nest making and oxytocin comparably promote wound healing in isolation reared rats. *PLoS ONE*, *4*(5), e5523. https://doi.org/10.1371/journal.pone.0005523

Volk, S. W., & Bohling, M. W. (2013). Comparative wound healing—Are the small animal veterinarian's clinical patients an improved translational model for human wound healing research?. *Wound Repair and Regeneration*, *21*(3), 372-381. https://doi.org/10.1111/wrr.12049

Volkers, K. M., & Scherder, E. J. (2011). Impoverished environment, cognition, aging and dementia. *Reviews in the Neurosciences*, *22*(3), 259-266. https://doi.org/10.1515/rns.2011.026

Vozzella, S. (2007). Sensory stimulation in dementia care: Why it is important and how to implement it. *Topics in Geriatric Rehabilitation*, *23*(2), 102-113. https://doi.org/10.1097/01.TGR.0000270179.23952.23

Wada, K., Shibata, T., Saito, T., Sakamoto, K., & Tanie, K. (2005). Psychological and social effects of one year robot assisted activity on elderly people at a health service facility for the aged. In *Proceedings of the 2005 IEEE International Conference On Robotics And Automation* (pp. 2785-2790). IEEE. http://doi.org/10.1109/ROBOT.2005.1570535

Wada, K., Shibata, T., Sakamoto, K., & Tanie, K. (2006). Long-term interaction between seal robots and elderly people. Robot assisted activity at a health service facility for the aged. In K. Murase, K. Sekiyama, T. Naniwa, N. Kubota, & J. Sitte (Eds.) *Proceedings of the 3rd International Symposium on Autonomous Minirobots for Research and Edutainment* (pp. 325-330). Springer. https://doi.org/10.1007/3-540-29344-2_48

Walburn, J., Vedhara, K., Hankins, M., Rixon, L., & Weinman, J. (2009). Psychological stress and wound healing in humans: A systematic review and meta-analysis. *Journal of Psychosomatic Research*, *67*(3), 253-271. https://doi.org/10.1016/j.jpsychores.2009.04.002

Wang, T., Mo, L., Vartanian, O., Cant, J. S., & Cupchik, G. (2015). An investigation of the neural substrates of mind wandering induced by viewing traditional Chinese landscape paintings. *Frontiers in Human Neuroscience*, *8*, 1018. https://doi.org/10.3389/fnhum.2014.01018

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology*, *54*(6), 1063-1070. https://doi.org/10.1037/0022-3514.54.6.1063

Weinman, J., Ebrecht, M., Scott, S., Walburn, J., & Dyson, M. (2008). Enhanced wound healing after emotional disclosure intervention. *British Journal of Health Psychology, 13*(1), 95-102. https://doi.org/10.1348/135910707X251207

Weiss, G., Shemer, A., & Trau, H. (2002). The koebner phenomenon: Review of the literature. *Journal of the European Academy of Dermatology and Venereology, 16*(3), 241-248. https://doi.org/10.1046/j.1473-2165.2002.00406.x

Weitlauf, A. S., Sathe, N., McPheeters, M. L., & Warren, Z. E. (2017). Interventions targeting sensory challenges in autism spectrum disorder: A systematic review. *Pediatrics, 139*(6), e20170347. https://doi.org/10.1542/peds.2017-0347

White, J. H., Bartley, E., Janssen, H., Jordan, L. A., & Spratt, N. (2015). Exploring stroke survivor experience of participation in an enriched environment: A qualitative study. *Disability and Rehabilitation*, *37*(7), 593-600. https://doi.org/10.3109/09638288.2014.935876

White, M. P., Alcock, I., Grellier, J., Wheeler, B. W., Hartig, T., Warber, S. L., Bone, A., Depledge, M. H., & Fleming, L. E. (2019). Spending at least 120 minutes a week in nature is associated with good health and wellbeing. *Scientific Reports, 9*(1), 7730. https://doi.org/10.1038/s41598-019-44097-3

White, M. P., Yeo, N. L., Vassiljev, P., Lundstedt, R., Wallergård, M., Albin, M., & Lõhmus, M. (2018). A prescription for "nature"—The potential of using virtual nature in therapeutics. *Neuropsychiatric Disease and Treatment*. *14*, 3001-3013. https://doi.org/10.2147/NDT.S179038

Wikström, B. M. (2011). The dynamics of visual art dialogues: Experiences to be used in hospital settings with visual art enrichment. *Nursing Research and Practice, 2011*, 1-7. https://doi.org/10.1155/2011/204594

Wikström, B. M., Theorell, T., & Sandström, S. (1993). Medical health and emotional effects of art stimulation in old age. *Psychotherapy and Psychosomatics*, *60*(3-4), 195-206. https://doi.org/10.1159/000288693

Wilhelm, K., Wilhelm, D., & Bielfeldt, S. (2017). Models of wound healing: An emphasis on clinical studies. *Skin Research and Technology, 23*(1), 3-12. https://doi.org/10.1111/srt.12317

Woo, C. C., Donnelly, J. H., Steinberg-Epstein, R., & Leon, M. (2015). Environmental enrichment as a therapy for autism: A clinical trial replication and extension. *Behavioral Neuroscience, 129*(4), 412-422. https://doi.org/10.1037/bne0000068

Woo, C. C., & Leon, M. (2013). Environmental enrichment as an effective treatment for autism: A randomized controlled trial. *Behavioral Neuroscience*, *127*(4), 487. https://doi.org/10.1037/a0033010

Wood, N., Sharkey, A., Mountain, G., & Millings, A. (2015). The Paro robot seal as a social mediator for healthy users. In M. Salem, A. Weiss, & P. Baxter, K. Dautenhahn (Eds.) *Proceedings of AISB Convention 2015, 4th International Symposium on New Frontiers*

in Human-Robot Interaction. The Society for the Study of Artificial Intelligence and the Simulation of Behaviour. http://eprints.whiterose.ac.uk/95993/

Wright, R. L., & Conrad, C. D. (2008). Enriched environment prevents chronic stress-induced spatial learning and memory deficits. *Behavioural Brain Research*, *187*(1), 41-47. https://doi.org/10.1016/j.bbr.2007.08.025

Xiao, Y., Zhang, X., Luo, D., Kuang, Y., Zhu, W., Chen, X., & Shen, M. (2019). The efficacy of psychological interventions on psoriasis treatment: A systematic review and meta-analysis of randomized controlled trials. *Psychology Research and Behavior Management*, *12*, 97-106. http://doi.org/10.2147/PRBM.S195181

Yang, H., & Zheng, J. (2019). Influence of stress on the development of psoriasis. *Clinical and Experimental Dermatology*, *45*(3), 284-288. https://doi.org/10.1111/ced.14105

Yehuda, N. (2011). Music and stress. *Journal of Adult Development*, *18*(2), 85-94. https://doi.org/10.1007/s10804-010-9117-4

Yu, L., Chiu, C. H., Lin, Y. S., Wang, H. H., & Chen, J. W. (2007). Testing a model of stress and health using meta-analytic path analysis. *Journal of Nursing Research*, *15*(3), 202-214. https://doi.org/10.1097/01.JNR.0000387616.64812.60

Zachariae, R., Øster, H., Bjerring, P., & Kragballe, K. (1996). Effects of psychologic intervention on psoriasis: A preliminary report. *Journal of the American Academy of Dermatology*, *34*(6), 1008-1015. https://doi.org/10.1016/S0190-9622(96)90280-7

Zachariae, R., Zachariae, H., Blomqvist, K., Davidsson, S., Molin, L., Mørk, C., & Sigurgeirsson, B. (2004). Self-reported stress reactivity and psoriasis-related stress of Nordic psoriasis sufferers. *Journal of the European Academy of Dermatology and Venereology*, *18*(1), 27-36. https://doi.org/10.1111/j.1468-3083.2004.00721.x

Zeanah, C. H., Egger, H. L., Smyke, A. T., Nelson, C. A., Fox, N. A., Marshall, P. J., & Guthrie, D. (2009). Institutional rearing and psychiatric disorders in Romanian preschool children. *American Journal of Psychiatry*, *166*(7), 777-785. https://doi.org/10.1176/appi.ajp.2009.08091438

Zhao, J., Lui, H., Kalia, S., & Zeng, H. (2015). Real-time Raman spectroscopy for automatic in vivo skin cancer detection: an independent validation. *Analytical and Bioanalytical Chemistry*, *407*(27), 8373-8379. https://doi.org/10.1007/s00216-015-8914-9

Zill, J. M., Christalle, E., Tillenburg, N., Mrowietz, U., Augustin, M., Härter, M., & Dirmaier, J. (2019). Effects of psychosocial interventions on patient-reported outcomes in patients with psoriasis: A systematic review and meta-analysis. *British Journal of Dermatology*, *181*(5), 939-945. https://doi.org/10.1111/bjd.17272

Appendix A: Study 1 Forms

Ethics Committee Approval Letter

Participant Information Sheet

Participant Consent Form

Questionnaire

Research Office
Post–Award Support Services

The University of Auckland
Private Bag 92019
Auckland, New Zealand

Level 10, 49 Symonds Street
Telephone: 64 9 373 7599
Extension: 83711
Facsimile: 64 9 373 7432
ro-ethics@auckland.ac.nz

UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE (UAHPEC)

28-Jul-2017

MEMORANDUM TO:

Dr Elizabeth Broadbent
Psychological Medicine

Re: Application for Ethics Approval (Our Ref. 019556): Approved

The Committee considered your application for ethics approval for your study entitled **Translating the Effects of Environmental Enrichment on Wound Healing to Human Populations**.

We are pleased to inform you that ethics approval has been granted for a period of three years.

The expiry date for this approval is 28-Jul-2020.

If the project changes significantly, you are required to submit a new application to UAHPEC for further consideration.

If you have obtained funding other than from UniServices, send a copy of this approval letter to the Activations team in the Research Office at ro-awards@auckland.ac.nz. For UniServices contracts, send a copy of the approval letter to the Contract Manager, UniServices.

The Chair and the members of UAHPEC would be happy to discuss general matters relating to ethics approvals. If you wish to do so, please contact the UAHPEC Ethics Administrators at ro-ethics@auckland.ac.nz in the first instance.

Please quote Protocol number **019556** on all communication with the UAHPEC regarding this application.

(This is a computer generated letter. No signature required.)

UAHPEC Administrators
University of Auckland Human Participants Ethics Committee

c.c. Head of Department / School, Psychological Medicine

Faculty of Medical and Health Sciences
The University of Auckland
Private Bag 92019
Auckland 1142
New Zealand

Environmental Enrichment and Wound Healing

PARTICIPANT INFORMATION SHEET

You are invited to take part in a research project investigating the effect of environmental enrichment on wound healing. You must be at least 16 years old to participate in this study.

This project is being supervised by Dr. Elizabeth Broadbent (Associate Professor in Health Psychology), co-supervised by Dr. Paul Jarrett (Consultant dermatologist, Middlemore Hospital) and carried out by Mikaela Law (PhD candidate).

It is important to read this document carefully so that you can make an informed decision about whether you would like to participate.

Procedure: If you are eligible for this intervention study and you would like to participate you will be asked to attend a one-off experimental session at the University of Auckland, Grafton Campus. The timing of this session will be arranged once you have confirmed your participation. Each session will take approximately 2 hours.

Tape Stripping. The study requires you to undergo a simple and non-invasive tape-stripping procedure on your forearm. During this procedure, strips of tape will be applied and gently peeled off the skin on your forearm in three 1cm^2 diameter areas just below your elbow in order to remove the topmost layer of your skin. This will be repeated 20-40 times with different strips of tape. The tape-stripping procedure is pain-free; however, you may experience mild discomfort, redness or itching. To ensure the right level of skin disruption is achieved, a small probe will be pressed gently against your skin for a few minutes per area. After a 30 minute recovery period, your skin barrier function will again be tested using this probe to examine how much your skin has recovered. During the recovery period you will be video-recorded.

Physiological measures. Saliva samples will be collected at three different time-points throughout the study; at baseline, after the tape stripping procedure and at the end of the study. These saliva samples will be analysed in order to examine levels of the hormones cortisol and alpha-amylase. The samples will be stored in Salicap containers in a secure lab in the University of Auckland at -20 degrees Celsius for up to 2 years. The samples may be sent

overseas to the University of Marburg (Germany) for analysis by a specialist laboratory. After the salivary samples have been analysed, they will be disposed of.

Questionnaires. During the experimental session you will be asked to complete a series of questionnaires pertaining to your general demographics, mood, health behaviours, stress levels and current pain.

Environmental enrichment. Upon beginning the study you will be randomised to either receive a form of environmental enrichment or not. The environmental enrichment that you will be given to interact with will be provided to you after the tape stripping procedure and during the recovery period to determine whether it may influence your rate of skin barrier recovery. It is very important that you engage with the item you are provided with for the purpose of this study. The researcher will not be in the room during this recovery period.

Your rights as a participant: Participation in this study is entirely voluntary. If you choose to participate, you can change your mind at any time, including during a session, without giving a reason and without any negative consequences. You may also withdraw your data up to two weeks after completing the study, in which case the data will be securely destroyed. You will be given a copy of this document to keep.

Koha: You will be reimbursed a $40 Westfield voucher at the conclusion of the experimental session as a koha for agreeing to participate in this research. You will receive this irrespective of whether you withdraw during the study.

Risks and discomforts: The procedures outlined in this protocol are minimally invasive and have been performed in other research settings. The tape-stripping procedure may cause slight discomfort and redness of the skin but this should disappear within 24 hours. If you have an allergy to cello tape or adhesives, an inflammatory skin disease or are taking medication that affects immune functioning, you should not take part in this research. If skin irritation persists, you should contact University Health Services on 09 923 7681 to make an appointment with a doctor or contact the researchers to organise to see the study dermatologist, Dr. Paul Jarrett, at no-charge.

Your researcher is not medically trained and therefore is unable to make any clinical observations about your physiological measures or mental states during the sessions. However, if any abnormal physiological or psychological recordings are made, you will be informed and will be provided with the contact details of the appropriate experts if required.

Confidentiality: Your data (questionnaire responses, wound healing rates and saliva samples) will be used to test the study's hypotheses. Statistical analyses will be performed, the results of which will then be discussed in research reports. Research publications and presentations from the study will not contain any information that could personally identify you, only averages will be presented.

Any information that identifies you as a participant will be used confidentially and kept in a secure location. Your name will appear only on your Consent Form, which will be coded with a

participation identification number. This identification number is used to de-identify all other data, ensuring your identity is kept confidential. Your data will only be referred to or labelled with this number. The Consent Form will only be seen by you and the researchers, and will be kept in a secure filing cabinet in the Department of Psychological Medicine at the University of Auckland for a period of 6 years to allow for publication and future analysis.

All data will be destroyed after a period of 6 years. This will be done by shredding physical data and deleting electronic data.

Results: A summary of the research's findings can be emailed to you upon request. As it takes some time to analyse the results of the study, it may be more than one year after your participation that you receive this summary.

Contact details: We appreciate the time you have taken to read this information. If you would like to participate or have any questions, please contact;

Mikaela Law
PhD Candidate, Department of Psychological Medicine,
The University of Auckland,
Private Bag 92019, Auckland 1142
Email: mlaw382@aucklanduni.ac.nz
Phone: (09) 373 7599 Ext. 89453

Alternative Contacts:
Dr. Elizabeth Broadbent, Department of Psychological Medicine,
The University of Auckland,
Private Bag 92019, Auckland 1142
Email: e.broadbent@auckland.ac.nz
Phone: (09) 373 7599 Ext. 86756

Or the **Head of the Department of Psychological Medicine, Professor Sally Merry.**
Email: s.merry@auckland.ac.nz
Phone: (09) 923 6981

For any queries regarding ethical concerns, contact the Chair, The University of Auckland Human Participants Ethics Committee, The University of Auckland, Office of the Vice Chancellor, Private Bag 92019, Auckland 1142. Telephone 09 373-7599 ext. 83711. Email: ro-ethics@auckland.ac.nz

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE
ON 28/07/2017 for 3 years, Reference Number 019556

Faculty of Medical and Health Sciences
The University of Auckland
Private Bag 92019
Auckland 1142
New Zealand

Environmental Enrichment and Wound Healing

PARTICIPANT CONSENT FORM

This form will be stored for a period of 6 years.

Researchers: Dr. Elizabeth Broadbent (Supervisor), Dr. Paul Jarrett (Co-supervisor) and Mikaela Law (PhD candidate)

- I have read the Participant Information Sheet, and have understood the nature of the research.
- I understand that participation in this study is voluntary and will take me approximately 2 hours to complete.
- I know that I am able to withdraw my participation at any time without giving an explanation and I can withdraw any data traceable up to two weeks after completing the study if I wish, in which case the data will be securely destroyed.
- I know who to contact if I have any questions about the study.
- I have had the opportunity to ask questions and have them answered to my satisfaction.
- I understand that my responses will be used for data analyses.
- I understand that participation in the study is confidential and that no material which could potentially identify me will be used in any reports or shared with any individual or organisation.
- I am aware that as a result of taking part in this study I will be given a $40 Westfield voucher as koha for agreeing to take part in this research, irrespective of whether I complete the study.
- I understand that during the experiment I will be subjected to a tape stripping procedure which may cause slight discomfort and redness of the skin but this should disappear within 24 hours. If skin irritation persists I understand I can contact University Health Services on 09 923 7681 to make an appointment with a doctor or contact the researchers to organise to see the study's dermatologist.
- I understand that my salivary samples will be stored securely at the University of Auckland at -20 degrees Celsius and may be sent to Germany for analysis after which they will be disposed of.
- I understand that throughout the experiment, I will complete a series of questionnaires, which include answering questions about my mood, health behaviours and demographics

- I understand that during the experimental session, some of my responses will be video-recorded
- I understand that the research data (including questionnaires, video-recordings, wound healing measurements and saliva samples) will be stored securely in the University of Auckland, Department Of Psychological Medicine for six years, after which it will be destroyed by shredding/deleting according to whether it is hard copy or electronic.
- I am not aware of any reason why I should not participate in this research

I agree to take part in this research.

Name…….

Signature……

Date……

☐ I wish to receive a summary of the research findings.

Please email me at: ……..

If you have any questions, please feel free to email the researchers at
mlaw382@aucklanduni.ac.nz

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE
ON 28/07/2017 for 3 years, Reference Number 019556

THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

MEDICAL AND HEALTH SCIENCES

Baseline Questionnaire

This questionnaire is designed to gather some background information on your demographics, as well as your feelings and mood. All of the information you give us is confidential to the researchers and will only be used for the purposes of the study.

For all these questions there are no right or wrong answers- an answer is correct if it is true for you. We are most interested in your own opinion. Please choose the response that best fits with your circumstances.

Thank you for your help with this study

Demographics Questionnaire

Please answer the following questions by filling in the blanks or ticking the circles that best correspond to you

1. What is your gender?
    - O Female
    - O Male
    - O Non-Binary/Other

2. How old are you? _____

3. Height _____cm

4. Weight _____kg

5. What ethnic group do you belong to? (check all that apply)
    - O New Zealand European/Pakeha
    - O Maori
    - O Samoan
    - O Cook Island Maori
    - O Tongan
    - O Chinese
    - O Indian
    - O Other: Please Specify _____

6. What is your highest level of completed education?
    - O Secondary school (up to and including year 11)
    - O Secondary school (including years 12 and 13)
    - O Technical or trade certificate
    - O University or polytechnic diploma
    - O Undergraduate University degree (e.g. Bachelor's degree)
    - O Postgraduate University degree- Honours
    - O Postgraduate University degree- Masters or PhD
    - O None of the above

7. What is your current employment status?
    - O Employed full time (40 or more hours per week)
    - O Employed part time (up to 39 hours per week)
    - O Student
    - O Not currently employed

Health- Related Behaviours

1. During the past three months how often have you drunk alcohol, on average?
    - O Not at all
    - O Less than once a month
    - O 1-3 times a month
    - O 1-2 times a week
    - O 3-6 times a week
    - O Every day

2. On the days when you did drink alcohol in the last three months, how many drinks did you have on an average day?
    - O 1-2 drinks
    - O 3-4 drinks
    - O 5-6 drinks
    - O 7-10 drinks
    - O 11 or more drinks
    - O N/A

3. During your average week, how many days do you engage in 30 minutes or more of physical activity (e.g. going for a walk or run, going to the gym, swimming)?
    - O Never
    - O 1 day
    - O 2 days
    - O 3 days
    - O 4 days
    - O 5 days
    - O 6 days
    - O Every day

4. During the past week, how would you rate your diet?
    - O Very poor
    - O Poor
    - O Fair
    - O Good
    - O Very good

5. Do you currently smoke?
    - O Yes. On an average day I smoke _____ cigarettes
    - O No, not anymore. I quit smoking _____ ago
    - O No, I have never smoked

6. Are you currently on any regular medication Yes/No
   If yes, please indicate the name of the medication(s)
   _____
   _____
   _____

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month.

7. During the past month, what time have you usually gone to bed at night?
   _____ O'Clock

8. During the past month, what time have you usually woken up in the morning?
   _____ O'Clock

9. During the past month, how many hours of actual sleep did you get per night? (this may be different than the number of hours you spent in bed)
   _____hours of sleep per night

10. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?
    _____ minutes

11. During the past month, how often have you had trouble sleeping because you cannot get to sleep within 30 minutes?
    - O Not during the past month
    - O Less than once a week
    - O Once or twice a week
    - O Three or more times a week

12. During the past month, how would you rate your quality of sleep?
    - O Very bad
    - O Fairly bad
    - O Fairly good
    - O Very good

The following 2 questions are for females only

1. On what date did you last experience menstrual bleeding?

   _____

   N/A

2. Are you currently using hormonal contraceptives? Yes / No

   If yes, please indicate the name of the medication

   _____

Over the last 2 weeks, how often have you been bothered by any of the following problems? Please circle the appropriate number

	Not at all	**Several days**	**More than half the days**	**Nearly every day**
1- Little interest or pleasure in doing things	1	2	3	4
2- Feeling down, depressed or hopeless	1	2	3	4
3- Trouble falling or staying asleep, or sleeping too much	1	2	3	4
4- Feeling tired or having little energy	1	2	3	4
5- Poor appetite or overeating	1	2	3	4
6- Feeling bad about yourself- or that you are a failure, or have let yourself or your family down	1	2	3	4
7- Trouble concentrating on things, such as reading or watching TV	1	2	3	4
8- Moving or speaking so slowly that other people could have noticed? Or the opposite; being so fidgety or restless that you have been moving around a lot more than usual	1	2	3	4
9- Thoughts that you would be better off dead or off hurting yourself in some way	1	2	3	4

If you checked off <u>any</u> of the 9 problems above, how <u>difficult</u> have these problems made it for you to do your work, take care of things at home, or get along with other people?

- O Not at all difficult
- O Somewhat difficult
- O Very difficult
- O Extremely difficult

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate how often you felt or thought a certain way by circling the appropriate number

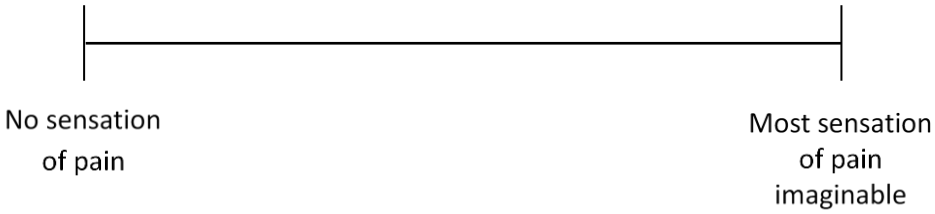
	Never	Almost Never	Some-times	Fairly Often	Very Often
1- In the last month, how often have you been upset because of something that happened unexpectedly?	**1**	**2**	**3**	**4**	**5**
2- In the last month, how often have you felt that you were unable to control the important things in your life?	1	2	3	4	5
3- In the last month, how often have you felt nervous and "stressed"?	1	2	3	4	5
4- In the last month, how often have you felt confident about your ability to handle your personal problems?	1	2	3	4	5
5- In the last month, how often have you felt that things were going your way?	1	2	3	4	5
6- In the last month, how often have you found that you could not cope with all the things that you had to do?	1	2	3	4	5
7- In the last month, how often have you been able to control irritations in your life?	1	2	3	4	5
8- In the last month, how often have you felt that you were on top of things?	1	2	3	4	5
9- In the last month, how often have you been angered because of things that were outside of your control?	1	2	3	4	5
10- In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	1	2	3	4	5

Listed below are a number of words that describe feelings. Some of the feelings are very similar to each other, whereas others are very different from each other. Read each word and then rate how much you feel that emotion right now by circling the appropriate number.

	Not at all	A little	Moderately	Quite a bit	Extremely
Still	1	2	3	4	5
Dull	1	2	3	4	5
Excited	1	2	3	4	5
Hostile	1	2	3	4	5
Strong	1	2	3	4	5
Sluggish	1	2	3	4	5
Aroused	1	2	3	4	5
Rested	1	2	3	4	5
Astonished	1	2	3	4	5
Quiet	1	2	3	4	5
Surprised	1	2	3	4	5
Enthusiastic	1	2	3	4	5
Passive	1	2	3	4	5
Fearful	1	2	3	4	5
Sad	1	2	3	4	5
Sleepy	1	2	3	4	5
Peaceful	1	2	3	4	5
Nervous	1	2	3	4	5
Relaxed	1	2	3	4	5
Lonely	1	2	3	4	5
Content	1	2	3	4	5
Calm	1	2	3	4	5
Happy	1	2	3	4	5
Unhappy	1	2	3	4	5
Satisfied	1	2	3	4	5

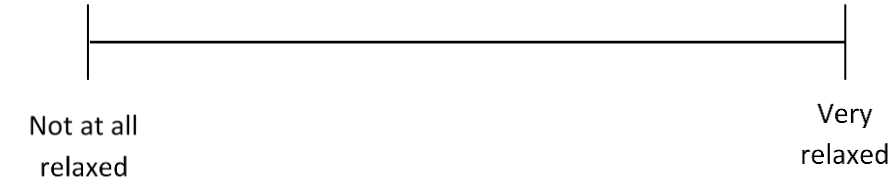
Please rate your current level of stress on the scale below by putting an X on the appropriate place on the line.

Please rate how much pain you are currently experiencing on the scale below by putting an X on the appropriate place on the line.



Please rate how anxious you currently feel on the scale below by putting an X on the appropriate place on the line.

Please rate how relaxed you currently feel on the scale below by putting an X on the appropriate place on the line.



Please rate how stimulated/bored you currently feel on the scale below by putting an X on the appropriate place on the line.

Appendix B: Study 2 Forms

Ethics Committee Approval Letter

Participant Information Sheet

Participant Consent Form

Questionnaire

Research Office
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UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE (UAHPEC)

08-May-2018

MEMORANDUM TO:

Dr Elizabeth Broadbent
Psychological Medicine

Re: Application for Ethics Approval (Our Ref. 021058): Approved with comment

The Committee considered your application for ethics approval for your study entitled **Environmental Enrichment, Stress and Skin Healing**.

Ethics approval was given for a period of three years with the following comment(s):

1. PIS
Please add to the PIS that participants will need to turn off their phones and place all their belongings in an assigned, secure drawer.

The expiry date for this approval is 02-May-2021.

If the project changes significantly you are required to resubmit a new application to UAHPEC for further consideration.

If you have obtained funding other than from UniServices, send a copy of this approval letter to the Activations team in the Research Office, at ro-awards@auckland.ac.nz. For UniServices contracts, send a copy of the approval letter to the Contract Manager, UniServices.

The Chair and the members of UAHPEC would be happy to discuss general matters relating to ethics approvals if you wish to do so. Contact should be made through the UAHPEC Ethics Administrators at ro-ethics@auckland.ac.nz in the first instance.

Please quote Protocol number **021058** on all communication with the UAHPEC regarding this application.

Faculty of Medical and Health Sciences
The University of Auckland
Private Bag 92019
Auckland 1142
New Zealand

Environmental Enrichment, Stress and Wound Healing

PARTICIPANT INFORMATION SHEET

You are invited to take part in a research project investigating the effect of environmental enrichment and stress on wound healing. You must be at least 16 years old to participate in this study. We are looking for 90 participants to partake in this study.

This project is being supervised by Dr. Elizabeth Broadbent (Associate Professor in Health Psychology), co-supervised by Dr. Paul Jarrett (Consultant dermatologist, Middlemore Hospital) and carried out by Mikaela Law (PhD candidate in Health Psychology).

It is important to read this document carefully so that you can make an informed decision about whether you would like to participate.

Procedure: If you are eligible for this intervention study and you would like to participate you will be asked to attend a one-off experimental session at the University of Auckland, Grafton Campus. The timing of this session will be arranged once you have confirmed your participation. Each session will take approximately 2-2.5 hours. You will need to turn off your phones and place all your belongings in a secure drawer during the experimental session.

Tape Stripping. The study requires you to undergo a simple and non-invasive tape-stripping procedure on your forearm. During this procedure, strips of tape will be applied and gently peeled off the skin on your forearm in three 1cm^2 diameter areas just below your elbow in order to remove the topmost layer of your skin. This will be repeated 10-40 times with different strips of tape. The tape-stripping procedure is pain-free; however, you may experience mild discomfort, redness or itching. To ensure the right level of skin disruption is achieved, a small probe will be pressed gently against your skin for a few minutes per area. After a 30 minute recovery period, your skin barrier function will again be tested using this probe to examine how much your skin has recovered.

Physiological measures. Saliva samples will be collected at four different time-points throughout the study; at baseline, before and after the tape stripping procedure and at the end of the study. These saliva samples will be analysed in order to examine levels of the hormones cortisol and alpha-amylase. The samples will be stored in Salicap containers in a secure lab in the University of Auckland at -20 degrees Celsius for up to 2 years. The samples may be sent overseas to the University of Marburg (Germany) for analysis by a specialist laboratory. The samples may be stored

there for up to one year before analysis. After the salivary samples have been analysed, they will be disposed.

Questionnaires. During the experimental session you will be asked to complete a series of questionnaires pertaining to your general demographics, mood, health behaviours, stress levels and current pain. You don't have to answer a question if you feel uncomfortable doing so.

Environmental enrichment. Upon beginning the study you will be randomised to either receive a form of environmental enrichment or not. It is very important that you engage with the item you are provided with for the purpose of this study.

Speech Task. During the procedure, you will be exposed to a speech task. During this task, you will be assigned a topic and given 3 minutes to prepare and 5 minutes to present a speech which will be recorded by a video camera. Your performance on this speech will be rated after the completion of the study by a panel of judges and you will have a chance to win a $100 Westfield voucher based on your performance.

Your rights as a participant: Participation in this study is entirely voluntary. If you choose to participate, you can change your mind at any time, including during a session, without giving a reason and without any negative consequences. You may also withdraw your data up to two weeks after completing the study, in which case the data will be securely destroyed. You will be given a copy of this document to keep.

If a student of the University of Auckland, your grades and your relationship to the University will not be affected by your participation or non-participation.

Koha: You will be reimbursed a $40 Westfield voucher at the conclusion of the experimental session as a koha for agreeing to participate in this research. You will receive this irrespective of whether you withdraw during the study.

Risks and discomforts: The procedures outlined in this protocol are minimally invasive and have been performed in other research settings. The tape-stripping procedure may cause slight discomfort and redness of the skin but this should disappear within 24 hours. If you have an allergy to tape or adhesives, an inflammatory skin disease or are taking medication that affects immune functioning, you should not take part in this research. You also cannot take part in this research if you are pregnant. If skin irritation persists, you should contact University Health Services on 09 923 7681 to make an appointment with a doctor, contact your own GP or contact the researchers to organise to see the study dermatologist, Dr. Paul Jarrett, at no-charge.

Your researcher is not medically trained and therefore is unable to make any clinical observations about your physiological measures or mental states during the sessions. However, if any abnormal physiological or psychological recordings are made, you will be informed and will be provided with the contact details of the appropriate experts if required.

Confidentiality: Your data (questionnaire responses, wound healing rates and saliva samples) will be used to test the study's hypotheses. Statistical analyses will be performed, the results of which will then be discussed in research reports. Research publications and presentations from the study will not contain any information that could personally identify you, only averages will be presented.

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All data will be destroyed after a period of 6 years. This will be done by shredding physical data and deleting electronic data.

Results: A summary of the research's findings can be emailed to you upon request. As it takes some time to analyse the results of the study, it may be more than one year after your participation that you receive this summary.

Contact details: We appreciate the time you have taken to read this information. If you would like to participate or have any questions, please contact;

Mikaela Law
PhD Candidate, Department of Psychological Medicine,
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Alternative Contacts:
Dr. Elizabeth Broadbent, Department of Psychological Medicine,
The University of Auckland,
Private Bag 92019, Auckland 1142
Email: e.broadbent@auckland.ac.nz
Phone: (09) 373 7599 Ext. 86756

Or the **Head of the Department of Psychological Medicine, Professor Sally Merry.**
Email: s.merry@auckland.ac.nz
Phone: (09) 923 6981

For any queries regarding ethical concerns, contact the Chair, The University of Auckland Human Participants Ethics Committee, The University of Auckland, Office of the Vice Chancellor, Private Bag 92019, Auckland 1142. Telephone 09 373-7599 ext. 83711. Email: ro-ethics@auckland.ac.nz

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE ON 02/05/2018 for 3 years, Reference Number 021058

MEDICAL AND HEALTH SCIENCES

Environmental Enrichment, Stress and Wound Healing

PARTICIPANT CONSENT FORM

This form will be stored for a period of 6 years.
Researchers: Dr. Elizabeth Broadbent (Supervisor), Dr. Paul Jarrett (Co-supervisor) and Mikaela Law (PhD candidate)

- I have read the Participant Information Sheet and have understood the nature of the research.
- I understand that participation in this study is voluntary and will take me approximately 2-2.5 hours to complete.
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- I am aware that as a result of taking part in this study I will be given a $40 Westfield voucher as koha for agreeing to take part in this research, irrespective of whether I complete the study.
- I understand that during the experiment I will be subjected to a tape stripping procedure which may cause slight discomfort and redness of the skin but this should disappear within 24 hours. If skin irritation persists I understand I can contact University Health Services on 09 923 7681 to make an appointment with a doctor or contact the researchers to organise to see the study's dermatologist.
- I understand that I will participate in a speech task and have the chance to win a $100 Westfield voucher based off my performance.
- I understand that my saliva samples will be stored securely at the University of Auckland at -20 degrees Celsius and may be sent to Germany for analysis after which they will be disposed of.
- I understand that throughout the experiment, I will complete a series of questionnaires, which include answering questions about my mood, health behaviours and demographics
- I understand that during the experimental session, some of my responses will be video-recorded
- I understand that the research data (including questionnaires, video-recordings, wound healing measurements and saliva samples) will be stored securely in the University of Auckland, Department of Psychological Medicine for six years, after which it will be destroyed by shredding/deleting according to whether it is hard copy or electronic.
- I am aware that my grades will not be affected by my participation/ non-participation
- I am not aware of any reason why I should not participate in this research

I agree to take part in this research.

Name…… Signature……

Date……

☐ I wish to receive a summary of the research findings.

Please email me at: ……..

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE ON 02/05/2018 for 3 years, Reference Number 021058

THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

MEDICAL AND HEALTH SCIENCES

Baseline Questionnaire

This questionnaire is designed to gather some background information on your demographics, as well as your feelings and mood. All of the information you give us is confidential to the researchers and will only be used for the purposes of the study.

For all these questions there are no right or wrong answers- an answer is correct if it is true for you. We are most interested in your own opinion. Please choose the response that best fits with your circumstances.

Demographics Questionnaire

Please answer the following questions by filling in the blanks or ticking the circles that best correspond to you

8. What is your gender?
    - O Female
    - O Male
    - O Gender diverse

9. How old are you? _____

10. Height _____cm

11. Weight _____kg

12. What ethnic group do you belong to? (check all that apply)
    - O New Zealand European/Pakeha
    - O Maori
    - O Samoan
    - O Cook Island Maori
    - O Tongan
    - O Chinese
    - O Indian
    - O Other: Please Specify _____

13. What is your highest level of **completed** education?
    - O Secondary school (up to and including year 11)
    - O Secondary school (including years 12 and 13)
    - O Technical or trade certificate
    - O University or polytechnic diploma
    - O Undergraduate University degree (e.g. Bachelor's degree)
    - O Postgraduate University degree- Honours
    - O Postgraduate University degree- Masters or PhD
    - O None of the above

14. What is your current employment status? (Please select only 1)
    - O Employed full time (40 or more hours per week)
    - O Employed part time (up to 39 hours per week)
    - O Student
    - O Not currently employed

Health- Related Behaviours

13. During the past three months how often have you drunk alcohol, on average?
    - O Not at all
    - O Less than once a month
    - O 1-3 times a month
    - O 1-2 times a week
    - O 3-6 times a week
    - O Every day

14. On the days when you did drink alcohol in the last three months, how many drinks did you have on an average day?
    - O 1-2 drinks
    - O 3-4 drinks
    - O 5-6 drinks
    - O 7-10 drinks
    - O 11 or more drinks
    - O N/A

15. During your average week, how many days do you engage in 30 minutes or more of physical activity (e.g. going for a walk or run, going to the gym, swimming)?
    - O Never
    - O 1 day
    - O 2 days
    - O 3 days
    - O 4 days
    - O 5 days
    - O 6 days
    - O Every day

16. During the past week, how would you rate your diet?
    - O Very poor
    - O Poor
    - O Fair
    - O Good
    - O Very good

17. Do you currently smoke?
    - O Yes. On an average day I smoke _____ cigarettes
    - O No, not anymore. I quit smoking _____ ago
    - O No, I have never smoked

18. Are you currently on any regular medication Yes/No
    If yes, please indicate the name of the medication(s)

    _____
    _____
    _____

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month.

19. During the past month, what time have you usually gone to bed at night?
    _____ O'Clock

20. During the past month, what time have you usually woken up in the morning?
    _____ O'Clock

21. During the past month, how many hours of actual sleep did you get per night? (this may be different than the number of hours you spent in bed)
    _____hours of sleep per night

22. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?
    _____ minutes

23. During the past month, how often have you had trouble sleeping because you cannot get to sleep within 30 minutes?
    - O Not during the past month
    - O Less than once a week
    - O Once or twice a week
    - O Three or more times a week

24. During the past month, how would you rate your quality of sleep?
    - O Very bad
    - O Fairly bad
    - O Fairly good
    - O Very good

The following questions relate to your sleep <u>LAST NIGHT</u>.

25. How many hours of sleep have you had <u>over the last 24 hours</u>? (This includes time spent napping)

    _____hours

26. How would you rate your sleep quality overall last night?
    - O Very bad
    - O Fairly bad
    - O Fairly good
    - O Very good

The following 2 questions are for females only

3. On what date was the first day of your most recent menstrual cycle?

_____

N/A

4. Are you currently using hormonal contraceptives/birth control? Yes / No

If yes, please indicate the name of the medication

_____

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate how often you felt or thought a certain way by circling the appropriate number

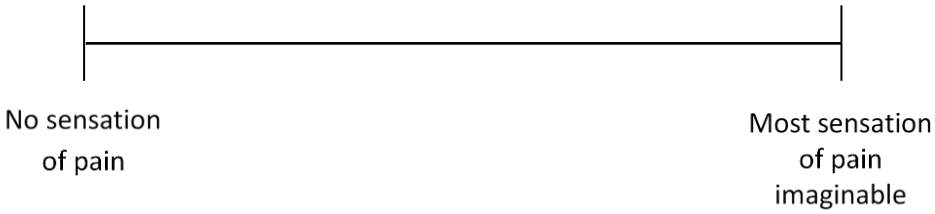
	Never	Almost Never	Some-times	Fairly Often	Very Often
1- In the last month, how often have you been upset because of something that happened unexpectedly?	0	1	2	3	4
2- In the last month, how often have you felt that you were unable to control the important things in your life?	0	1	2	3	4
3- In the last month, how often have you felt nervous and "stressed"?	0	1	2	3	4
4- In the last month, how often have you felt confident about your ability to handle your personal problems?	0	1	2	3	4
5- In the last month, how often have you felt that things were going your way?	0	1	2	3	4
6- In the last month, how often have you found that you could not cope with all the things that you had to do?	0	1	2	3	4
7- In the last month, how often have you been able to control irritations in your life?	0	1	2	3	4
8- In the last month, how often have you felt that you were on top of things?	0	1	2	3	4
9- In the last month, how often have you been angered because of things that were outside of your control?	0	1	2	3	4
10- In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	0	1	2	3	4

Listed below are a number of words that describe feelings. Some of the feelings are very similar to each other, whereas others are very different from each other. Read each word and then rate how much you feel that emotion right now by circling the appropriate number.

	Not at all	A little	Moderately	Quite a bit	Extremely
Still	1	2	3	4	5
Dull	1	2	3	4	5
Excited	1	2	3	4	5
Hostile	1	2	3	4	5
Strong	1	2	3	4	5
Sluggish	1	2	3	4	5
Aroused	1	2	3	4	5
Rested	1	2	3	4	5
Astonished	1	2	3	4	5
Quiet	1	2	3	4	5
Surprised	1	2	3	4	5
Enthusiastic	1	2	3	4	5
Passive	1	2	3	4	5
Fearful	1	2	3	4	5
Sad	1	2	3	4	5
Sleepy	1	2	3	4	5
Peaceful	1	2	3	4	5
Nervous	1	2	3	4	5
Relaxed	1	2	3	4	5
Lonely	1	2	3	4	5
Content	1	2	3	4	5
Calm	1	2	3	4	5
Happy	1	2	3	4	5
Unhappy	1	2	3	4	5
Satisfied	1	2	3	4	5

Please rate your current level of stress on the scale below by putting an X on the appropriate place on the line.

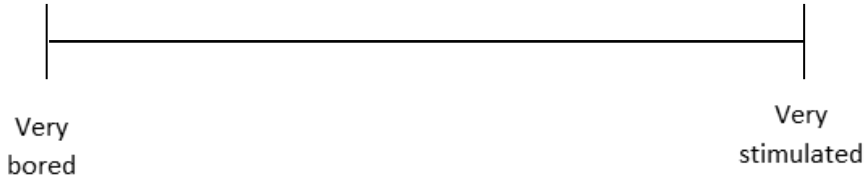
Please rate how much pain you are currently experiencing on the scale below by putting an X on the appropriate place on the line.



Please rate how anxious you currently feel on the scale below by putting an X on the appropriate place on the line.

Please rate how relaxed you currently feel on the scale below by putting an X on the appropriate place on the line.

Please rate how stimulated/bored you currently feel on the scale below by putting an X on the appropriate place on the line.



Appendix C: Study 3 Forms

Ethics Committee Approval Letter

Participant Information Sheet

Participant Consent Form

Questionnaire

Office of the Vice-Chancellor
Office of Research Strategy and Integrity (ORSI)

The University of Auckland
Private Bag 92019
Auckland, New Zealand

Level 11, 49 Symonds Street
Telephone: 64 9 373 7599
Extension: 83711
humanethics@auckland.ac.nz

UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE (UAHPEC)

27-Jun-2019

MEMORANDUM TO:

Dr Elizabeth Broadbent
Psychological Medicine

Re: Application for Ethics Approval (Our Ref. 023106): Approved with comment

The Committee considered your application for ethics approval for your study entitled: **The Effect of Environmental Enrichment and Stress on Psoriasis**.

We are pleased to inform you that ethics approval has been granted for a period of three years with the following comment(s) or required minor change(s):

The committee would like to thank the applicants for a well written application

The expiry date for this approval is 27-Jun-2022.

Completion of the project: In order that up-to-date records are maintained, you must notify the Committee once your project is completed.

Amendments to the project: Should you need to make any changes to the project, please complete an Amendment Request form giving full details along with revised documentation. If the project changes significantly, you are required to submit a new application to UAHPEC for approval.

Funded projects: If you received funding for this project, please provide the approval letter to your local Faculty Research Project Coordinator (RPC) or Research Project Manager (RPM) so that the approval can be notified via a Service Request to the Research Operations Centre (ROC) for activation of the grant.

The Chair and the members of UAHPEC would be happy to discuss general matters relating to ethics approvals if you wish to do so. please contact the UAHPEC Ethics Administrators at humanethics@auckland.ac.nz in the first instance.

Additional information:

1. Do not forget to complete the 'approval wording' on the PISs, CFs and/or advertisements and emails, giving the dates of approval and the reference number. This needs to be completed before you use the documents or

Faculty of Medical and Health Sciences
The University of Auckland
Private Bag 92019
Auckland 1142
New Zealand

The Effect of Environmental Enrichment and Stress on Psoriasis

PARTICIPANT INFORMATION SHEET

You are invited to take part in a research project investigating the effect of environmental enrichment and stress on psoriasis. We are looking for 76 participants with chronic plaque psoriasis to participate in this study.

This project is being supervised by Professor Elizabeth Broadbent (Professor in Health Psychology), co-supervised by Dr. Paul Jarrett (Consultant dermatologist, Middlemore Hospital and the Department of Medicine) and carried out by Mikaela Law (PhD candidate in Health Psychology). The research is also supported by Dr. Michel Nieuwoudt (Senior Research Fellow in Chemical Sciences) and Hannah Holtkamp (Post-Doctoral Fellow in Chemical Sciences).

It is important to read this document carefully so that you can make an informed decision about whether you would like to participate.

Eligibility: For this project you must fit a number of inclusion criteria. These include:

- Diagnosis of chronic stable plaque psoriasis
- Over the age of 16 years
- Fluent in English
- No other significant skin conditions
- Not currently taking any systemic (oral) therapy for psoriasis including cyclosporin, methotrexate, acitretin, or concurrent phototherapy or biologic agents. You must have been off all systemic psoriasis treatments for at least 3 months to be eligible to participate
- Not on any other immunosuppressive medications
- No recent or anticipated changes in anti-depressant or anxiolytic medications

If you are unsure if you fit these eligibility criteria, you can still attend the first screening session to be assessed by the study dermatologist and have a free skin-check.

Procedure: If you believe you are eligible for this intervention study and you would like to participate you will be asked to attend two sessions at the University of Auckland, Grafton Campus; a screening visit and an experimental session.

Screening Visit: the screening visit will take approximately 20 minutes of your time. During this visit, Dr. Paul Jarrett, a dermatologist, will conduct a free skin check to assess your psoriasis to see if you fit the inclusion criteria listed above. If eligible for the study, Dr. Jarrett will select a psoriatic plaque to be measured in the second session. This plaque will preferably be on your arm, leg or torso. The dermatologist will photograph and measure this plaque. You will be asked to refrain from treating this plaque with topical treatments until after your experimental session has been completed. The lead researcher will be in contact with you after this screening visit to arrange a time for the second, experimental session which will be held between 1 to 4 weeks after the screening visit, at a time that suits you best.

Experimental Session: The experimental session will last approximately 2 hours. During this session you will be exposed to a number of tasks and your selected psoriatic lesion will be measured to assess any changes across the session. You will need to turn off your phones and place all your belongings in a secure place during the experimental session.

Psoriasis Measurements. Your selected psoriatic plaque will be measured three times throughout the session. During these measurements, you will be asked to lie on a bed, with your selected plaque uncovered. A $1cm^2$ site will be marked out on both your plaque, and on a control site of healthy skin nearby. The researcher will then measure each of these sites using two non-invasive devices: a Tewameter and a Raman spectroscopy device. The Tewameter measures the water content of your skin. It will be placed against your skin and will measure each site for up to 90 seconds. The Raman spectroscopy device focuses a laser of low power on your skin to measure the biomolecular composition of the skin. This device will measure each of the two sites for approximately 1 to 2 minutes. Both of these measurements are non-invasive and completely harmless. The laser light of the Raman device is approximately half the American National Standards Institute (ANSI) Z136 maximum permitted exposure for laser light on skin. You will also be issued with laser safety glasses as an added precaution; however, the chances are minimal that your eyes would be exposed to any laser radiation.

Questionnaires. During the experimental session you will be asked to complete a series of questionnaires pertaining to your general demographics, mood, health behaviours, stress levels and current pain. You will also be asked a series of questions about your psoriasis. You don't have to answer a question if you feel uncomfortable doing so.

Speech task. During the procedure, you will be exposed to a speech task. During this task, you will be assigned a topic and given 3 minutes to prepare and 5 minutes to present a speech which will be recorded by a video camera. Your performance on this speech will be rated after the completion of the study by a panel of judges and you will have a chance to win a $100 Westfield voucher based on your performance.

Recovery period. After the speech task, you will have a 30 minute recovery period, before the final measures are completed, to assess your recovery from the stress task. During this 30 minutes, you will be randomised to one of two conditions which have differing amounts of enrichment. During this recovery period, you will be video-recorded to ensure compliance with instructions.

Your rights as a participant: Participation in this study is entirely voluntary. If you choose to participate, you can change your mind at any time, including during a session, without giving a

reason and without any negative consequences. You may also withdraw your data up to two weeks after completing the study, in which case the data will be securely destroyed. You will be given a copy of this document to keep. If a student of the University of Auckland, your grades and your relationship to the University will not be affected by your participation or non-participation.

Benefits: You will be reimbursed a $40 Westfield voucher at the conclusion of the second experimental session as a koha for agreeing to participate in this research. You will receive this irrespective of whether you withdraw during the study. You will also receive a skin check by a trained dermatologist, free of charge, at the first screening visit, to assess your psoriasis. At this session, the dermatologist can answer any questions you may have about your psoriasis. During the skin check, the dermatologist may find lesions that may be suspicious. In this event the dermatologist will inform you and provide you with a referral letter for your GP.

Risks and discomforts: Participants are not expected to experience any adverse consequences or physical or psychological risks from this study. If your psoriasis does become more severe after the stress task, you should contact University Health Services on 09 923 7681 to make an appointment with a doctor or contact your own GP.

Confidentiality: Your data (questionnaire responses, video-recordings and skin measures) will be used to test the study's hypotheses. Statistical analyses will be performed, the results of which will then be discussed in research reports. Research publications and presentations from the study will not contain any information that could personally identify you, only averages will be presented.

Any information that identifies you as a participant will be used confidentially and kept in a secure location. Your name will appear only on your Consent Form, which will be coded with a participation identification number. This identification number is used to de-identify all other data, ensuring your identity is kept confidential. Your data will only be referred to or labelled with this number. The Consent Form will only be seen by you and the researchers, and will be kept in a secure filing cabinet in the Department of Psychological Medicine at the University of Auckland for a period of 6 years to allow for publication and future analysis.

All data will be destroyed after a period of 6 years. This will be done by shredding physical data and deleting electronic data.

Results: A summary of the research's findings can be emailed to you upon request. As it takes some time to analyse the results of the study, it may be more than one year after your participation that you receive this summary.

Contact details: We appreciate the time you have taken to read this information. If you would like to participate or have any questions, please contact;

Mikaela Law
PhD Candidate, Department of Psychological Medicine,
The University of Auckland,
Private Bag 92019, Auckland 1142
Email: mlaw382@aucklanduni.ac.nz
Phone: (09) 373 7599 Ext. 89453
Alternative Contacts:

Professor Elizabeth Broadbent, Department of Psychological Medicine,
The University of Auckland,
Private Bag 92019, Auckland 1142
Email: e.broadbent@auckland.ac.nz
Phone: (09) 373 7599 Ext. 86756

Or the **Head of the Department of Psychological Medicine, Professor Sally Merry.**
Email: s.merry@auckland.ac.nz
Phone: (09) 923 6981

For any queries regarding ethical concerns, contact the Chair, The University of Auckland Human Participants Ethics Committee, The University of Auckland, Office of the Vice Chancellor, Private Bag 92019, Auckland 1142. Telephone 09 373-7599 ext. 83711. Email: ro-ethics@auckland.ac.nz

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE ON 27/06/2019 for 3 years, Reference Number 023106

MEDICAL AND HEALTH SCIENCES

The Effect of Environmental Enrichment and Stress on Psoriasis

PARTICIPANT CONSENT FORM

This form will be stored for a period of 6 years.
Researchers: Professor Elizabeth Broadbent (Supervisor), Dr. Paul Jarrett (Co-supervisor) and Mikaela Law (PhD candidate)

- I have read the Participant Information Sheet and have understood the nature of the research.
- I understand that participation in this study is voluntary and will involve two sessions, the first lasting approximately 20 minutes and the second, approximately 2 hours.
- I know that I am able to withdraw my participation at any time without giving an explanation and I can withdraw any data traceable up to two weeks after completing the study if I wish, in which case the data will be securely destroyed.
- I have had the opportunity to ask questions and have them answered to my satisfaction.
- I understand that my responses will be used for data analyses.
- I understand that participation in the study is confidential and that no material which could potentially identify me will be used in any reports or shared with any individual or organisation.
- I am aware that as a result of taking part in this study I will be given a $40 Westfield voucher as koha for agreeing to take part in this research, irrespective of whether I complete the study.
- I understand that I will participate in a speech task and have the chance to win a $100 Westfield voucher based on my performance.
- I understand that throughout the experiment, I will complete a series of questionnaires, which include answering questions about my mood, health behaviours, psoriasis and demographics.
- I understand that my skin (both healthy and psoriatic plaques) will be measured using two non-invasive devices throughout the experiment.
- I understand that there may be a possibility that the dermatological examination may find a skin abnormality. In such instances, the dermatologist will inform me and provide me with a referral letter to my GP.
- I understand that during the experimental session, some of my responses will be video-recorded.
- I understand that the research data (including questionnaires, video-recordings and skin measurements) will be stored securely in the University of Auckland, Department of Psychological Medicine for six years, after which it will be destroyed by shredding/deleting according to whether it is hard copy or electronic.
- If I am a University student, I am aware that my grades will not be affected by my participation/ non-participation.
- If I am a University staff member, I am aware that my employment with the university will not be affected by my participation/ non-participation.
- I am not aware of any reason why I should not participate in this research.

I agree to take part in this research.

Name…… Signature……

Date……

☐ I wish to receive a summary of the research findings.

Please email me at: ……

APPROVED BY THE UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE ON 27/06/2019 for 3 years, Reference Number 023106

THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

MEDICAL AND HEALTH SCIENCES

Baseline Questionnaire

This questionnaire is designed to gather some background information on your demographics, as well as your feelings and mood. All of the information you give us is confidential to the researchers and will only be used for the purposes of the study.

For all these questions there are no right or wrong answers- an answer is correct if it is true for you. We are most interested in your own opinion. Please choose the response that best fits with your circumstances.

Thank you for your help with this study

Demographics Questionnaire

Please answer the following questions by filling in the blanks or ticking the circles that best correspond to you

15. What is your gender?
    - O Female
    - O Male
    - O Gender diverse

16. How old are you? _____

17. Height _____cm

18. Weight _____kg

19. What ethnic group do you belong to? (check all that apply)
    - O New Zealand European/Pakeha
    - O Maori
    - O Samoan
    - O Cook Island Maori
    - O Tongan
    - O Chinese
    - O Indian
    - O Other: Please Specify _____

20. What is your highest level of **completed** education?
    - O Secondary school (up to and including year 11)
    - O Secondary school (including years 12 and 13)
    - O Technical or trade certificate
    - O University or polytechnic diploma
    - O Undergraduate University degree (e.g. Bachelor's degree)
    - O Postgraduate University degree- Honours
    - O Postgraduate University degree- Masters or PhD
    - O None of the above

21. What is your current employment status? (Please select only 1)
    - O Employed full time (40 or more hours per week)
    - O Employed part time (up to 39 hours per week)
    - O Student
    - O Not currently employed

Health- Related Behaviours

1. On average, how many standard alcoholic drinks do you consume per week
   - O 0 drinks
   - O 1-2 drinks
   - O 3-4 drinks
   - O 5-6 drinks
   - O 7-10 drinks
   - O 11 or more drinks

2. During your average week, how many days do you engage in 30 minutes or more of physical activity (e.g. going for a walk or run, going to the gym, swimming)?
   - O Never
   - O 1 day
   - O 2 days
   - O 3 days
   - O 4 days
   - O 5 days
   - O 6 days
   - O Every day

3. During the past week, how would you rate your diet?
   - O Very poor
   - O Poor
   - O Fair
   - O Good
   - O Very good

4. Are you currently a regular smoker?
   - O Yes. On an average day I smoke _____ cigarettes
   - O No, not anymore. I quit smoking _____ ago
   - O No, I have never been a regular smoker

5. Are you currently on any regular medication Yes/No
   If yes, please indicate the name of the medication(s)

   _____
   _____
   _____

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month.

27. During the past month, what time have you usually gone to bed at night?
    _____ O'Clock

28. During the past month, what time have you usually woken up in the morning?
    _____ O'Clock

29. During the past month, how many hours of actual sleep did you get per night? (this may be different than the number of hours you spent in bed)
    _____hours of sleep per night

30. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?
    _____ minutes

31. During the past month, how often have you had trouble sleeping because you cannot get to sleep within 30 minutes?
    - O Not during the past month
    - O Less than once a week
    - O Once or twice a week
    - O Three or more times a week

32. During the past month, how would you rate your quality of sleep?
    - O Very bad
    - O Fairly bad
    - O Fairly good
    - O Very good

Psoriasis Specific Questions

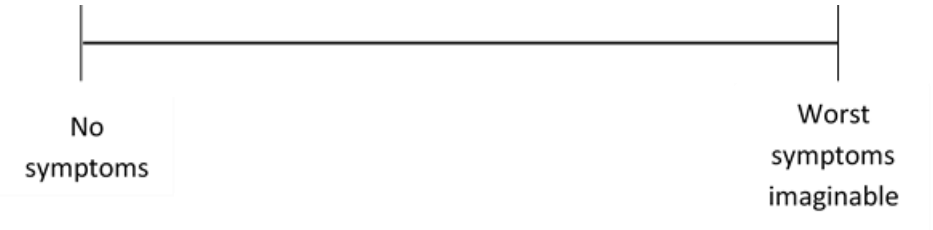
1. Approximately how many years have you had psoriasis?
   - O Less than 5 years
   - O 5-10 years
   - O 10-20 years
   - O More than 20 years

2. At what age did you experience your first psoriasis outbreak?
   - O 0-13
   - O 14-19
   - O 20-29
   - O Over 30

3. Do you believe that **stress** frequently worsens the severity of your psoriasis?
   - O Yes
   - O No
   - O Unsure

4. Have any of your parents or grandparents had psoriasis?
   - O Yes
   - O No
   - O Unsure

5. Please rate how severe you think your psoriasis currently is on the scale below by putting an X on the appropriate place on the line.



The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate how often you felt or thought a certain way by circling the appropriate number

	Never	Almost Never	Some-times	Fairly Often	Very Often
1- In the last month, how often have you been upset because of something that happened unexpectedly?	0	1	2	3	4
2- In the last month, how often have you felt that you were unable to control the important things in your life?	0	1	2	3	4
3- In the last month, how often have you felt nervous and "stressed"?	0	1	2	3	4
4- In the last month, how often have you felt confident about your ability to handle your personal problems?	0	1	2	3	4
5- In the last month, how often have you felt that things were going your way?	0	1	2	3	4
6- In the last month, how often have you found that you could not cope with all the things that you had to do?	0	1	2	3	4
7- In the last month, how often have you been able to control irritations in your life?	0	1	2	3	4
8- In the last month, how often have you felt that you were on top of things?	0	1	2	3	4
9- In the last month, how often have you been angered because of things that were outside of your control?	0	1	2	3	4
10- In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	0	1	2	3	4

Over the last 2 weeks, how often have you been bothered by any of the following problems? Please circle the appropriate number

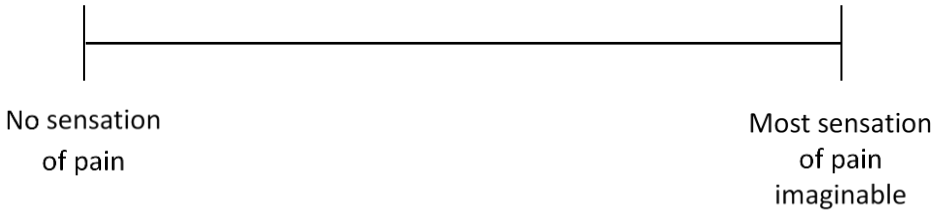
	Not at all	**Several days**	**More than half the days**	**Nearly every day**
1- Little interest or pleasure in doing things	1	2	3	4
2- Feeling down, depressed or hopeless	1	2	3	4
3- Trouble falling or staying asleep, or sleeping too much	1	2	3	4
4- Feeling tired or having little energy	1	2	3	4
5- Poor appetite or overeating	1	2	3	4
6- Feeling bad about yourself- or that you are a failure, or have let yourself or your family down	1	2	3	4
7- Trouble concentrating on things, such as reading or watching TV	1	2	3	4
8- Moving or speaking so slowly that other people could have noticed? Or the opposite; being so fidgety or restless that you have been moving around a lot more than usual	1	2	3	4
9- Thoughts that you would be better off dead or off hurting yourself in some way	1	2	3	4

This scale consists of a number of words that describe different feelings and emotions. Read each item and then circle the appropriate number to indicate to what extent you feel this way right now, at the present moment.

	Not at all	A little	Moderately	Quite a bit	Extremely
1. Interested	1	2	3	4	5
2. Distressed	1	2	3	4	5
3. Excited	1	2	3	4	5
4. Upset	1	2	3	4	5
5. Strong	1	2	3	4	5
6. Guilty	1	2	3	4	5
7. Scared	1	2	3	4	5
8. Hostile	1	2	3	4	5
9. Enthusiastic	1	2	3	4	5
10. Proud	1	2	3	4	5
11. Irritable	1	2	3	4	5
12. Alert	1	2	3	4	5
13. Ashamed	1	2	3	4	5
14. Inspired	1	2	3	4	5
15. Nervous	1	2	3	4	5
16. Determined	1	2	3	4	5
17. Attentive	1	2	3	4	5
18. Jittery	1	2	3	4	5
19. Active	1	2	3	4	5
20. Afraid	1	2	3	4	5

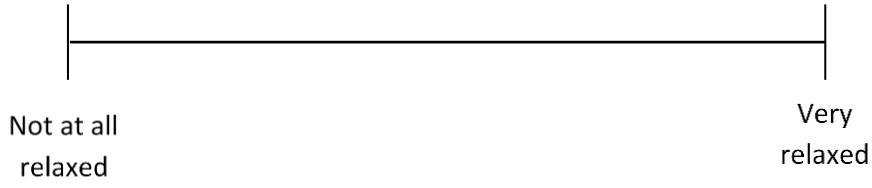
Please rate your current level of stress on the scale below by putting an X on the appropriate place on the line.

Please rate how much pain you are currently experiencing on the scale below by putting an X on the appropriate place on the line.



Please rate how anxious you currently feel on the scale below by putting an X on the appropriate place on the line.

Please rate how relaxed you currently feel on the scale below by putting an X on the appropriate place on the line.



Please rate how stimulated/bored you currently feel on the scale below by putting an X on the appropriate place on the line.

A number of statements which people have used to describe themselves are given below. Read each statement and circle the most appropriate number to indicate how you feel *right now, at this moment*.

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

Appendix D: Study 4 Forms

Ethics Committee Approval Letter

Participant Information Sheet

Participant Consent Form

Questionnaire

Research Office
Post–Award Support Services

The University of Auckland
Private Bag 92019
Auckland, New Zealand

Level 10, 49 Symonds Street
Telephone: 64 9 373 7599
Extension: 83711
Facsimile: 64 9 373 7432
ro-ethics@auckland.ac.nz

UNIVERSITY OF AUCKLAND HUMAN PARTICIPANTS ETHICS COMMITTEE (UAHPEC)

10-Oct-2017

MEMORANDUM TO:

Dr Gregory Minissale
Art History

Re: Application for Ethics Approval (Our Ref. 019958): Approved

The Committee considered your application for ethics approval for your study entitled **The Healing Power of Art**.

We are pleased to inform you that ethics approval has been granted for a period of three years.

The expiry date for this approval is 10-Oct-2020.

If the project changes significantly, you are required to submit a new application to UAHPEC for further consideration.

If you have obtained funding other than from UniServices, send a copy of this approval letter to the Activations team in the Research Office at ro-awards@auckland.ac.nz. For UniServices contracts, send a copy of the approval letter to the Contract Manager, UniServices.

The Chair and the members of UAHPEC would be happy to discuss general matters relating to ethics approvals. If you wish to do so, please contact the UAHPEC Ethics Administrators at ro-ethics@auckland.ac.nz in the first instance.

Please quote Protocol number **019958** on all communication with the UAHPEC regarding this application.

(This is a computer generated letter. No signature required.)

UAHPEC Administrators
University of Auckland Human Participants Ethics Committee

c.c. Head of Department / School, Art History

Faculty of Medical and Health Sciences
The University of Auckland
Private Bag 92019
Auckland 1142
New Zealand

The Healing Power of Art

PARTICIPANT INFORMATION SHEET

You are invited to take part in a research project investigating the effect of viewing art on reducing stress.

This project is being supervised by Dr Gregory Minissale (Art History), Tony Lambert (Associate Professor in Psychology), Dr. Elizabeth Broadbent (Associate Professor in Health Psychology), co-supervised by Mikaela Law (PhD candidate), carried out by Lenore Tahara-Eckl and Emma Holdaway (research assistants).

It is important to read this document carefully so that you can make an informed decision about whether you would like to participate.

Procedure: If you are eligible for this intervention study and you would like to participate you will be asked to attend a one-off experimental session at the University of Auckland, City Campus. The timing of this session will be arranged once you have confirmed your participation. Each session will take approximately 90 minutes.

The test endeavours to find out if viewing art, particularly landscape and abstract paintings, lowers physiological and psychological stress responses to a laboratory stress task faster than a control task (viewing scrambled images) during a rest or recovery period.

The Stress Test

You will have 3 minutes to prepare a speech on why you should be given your dream job: you will then have 3 minutes to present your speech to the video camera which will later be rated by a panel of experts. The best speech will be awarded a $100 Countdown voucher). Participants are then checked for stress levels (further details below) before going into a rest period for recovery.

Recovery Period

Art viewing. The art that you will be given to interact with will be provided to you as high quality image projections during the recovery period to determine whether it may influence your rate of recovery.

Looking at the art will take 20 minutes, as it takes 20 minutes for the cortisol response to occur. After 20 minutes there will be a saliva test and participants will look at more art for another 10 minutes and then we take one more saliva sample.

During this viewing period you will be fitted with an eye-tracking device to analyse your gaze while viewing the art.

Physiological measures. Saliva samples will be collected at four different time-points throughout the study. These saliva samples will be analysed in order to examine levels of the hormones cortisol and alpha-amylase. The samples will be stored in Salicap containers in a secure lab in the University of Auckland at -20 degrees Celsius for up to 2 years. The samples may be sent overseas to the University of Marburg (Germany) for analysis by a specialist laboratory. After the salivary samples have been analysed, they will be disposed of.

Questionnaires. During the experimental session you will be asked to complete a series of questionnaires pertaining to your general demographics, mood, health behaviours, stress levels and current pain.

Details on alcohol use, details about female participants' menstrual cycles and use of contraception are being collected. This information is being collected as all of these factors can affect the hormone concentrations within the participants' saliva and will therefore need to be controlled for in the statistical analysis of the salivary cortisol and alpha-amylase levels.

Your rights as a participant: Participation in this study is entirely voluntary. If you choose to participate, you can change your mind at any time, including during a session, without giving a reason and without any negative consequences. You may also withdraw your data up to one week after completing the study, in which case the data will be securely destroyed. You will be given a copy of this document to keep.

Koha: You will be reimbursed a $40 Countdown voucher at the conclusion of the experimental session as a koha for agreeing to participate in this research. You will receive this irrespective of whether you withdraw during the study.

Risks and discomforts:

There is no risk or discomfort involved. In the unlikely circumstance that a psychological disorder, such as clinical depression, is incidentally detected through the questionnaires used within the study, participants will be sent a letter and encouraged to contact a counselling service and given the contact details for the University of Auckland's free counselling services.

Should a heart rate or blood pressure recording be outside the usual range observed, the experimenter will terminate the experimental session and the participant will be advised to contact their General Practitioner to look further into the incidental finding.

Your researcher is not medically trained and therefore is unable to make any clinical observations about your physiological measures or mental states during the sessions. However, if any abnormal physiological or psychological recordings are made, you will be informed and will be provided with the contact details of the appropriate experts if required.

Confidentiality: Your data (questionnaire responses, eye tracking data and saliva samples) will be used to test the study's hypotheses. Statistical analyses will be performed, the results of which will then be discussed in research reports. Research publications and presentations from the study will not contain any information that could personally identify you, only averages will be presented.

Any information that identifies you as a participant will be used confidentially and kept in a secure location. Your name will appear only on your Consent Form, which will be coded with a participation identification number. This identification number is used to de-identify all other data, ensuring your identity is kept confidential. Your data will only be referred to or labelled with this number. The Consent Form will only be seen by you and the researchers, and will be kept in a secure filing cabinet in the Department of Psychological Medicine at the University of Auckland for a period of 6 years to allow for publication and future analysis.

All data will be destroyed after a period of 6 years. This will be done by shredding physical data and deleting electronic data.

Results: A summary of the research's findings can be emailed to you upon request. As it takes some time to analyse the results of the study, it may be more than one year after your participation that you receive this summary.

Exclusions

We will need to exclude any participants who cannot read or write in English fluently, who are under the age of 16 or who are pregnant (for the saliva samples). Pregnant woman are excluded from the entire study procedure as they have substantial differences in hormonal functions which would skew the results.

If you are a student of the researchers we give our assurance that your participation or non-participation in this study will have no effect on your grades or relationship with the University and that you may contact your HoD should you feel that this assurance has not been met.

Participants may contract Head of Department Psychological Medicine below if they feel that this assurance has not been met.

Contact details: We appreciate the time you have taken to read this information. If you would like to participate or have any questions, please contact;

Mikaela Law
PhD Candidate, Department of Psychological Medicine,
The University of Auckland,
Private Bag 92019, Auckland 1142
Email: mlaw382@aucklanduni.ac.nz
Phone: (09) 373 7599 Ext. 89453

Greg Minissale
Deputy Head (Research)
School of Humanities
University of Auckland
14A Symonds Street
Room 749, level 7, Arts 1
Auckland 1142, New Zealand
Email: g.minissale@auckland.ac.nz
Phone: (09) 923 7599 x 86033

Alternative Contacts:

Dr. Elizabeth Broadbent, Department of Psychological Medicine,
The University of Auckland,
Private Bag 92019, Auckland 1142
Email: e.broadbent@auckland.ac.nz
Phone: (09) 373 7599 Ext. 86756

Prof Sally Merry
Head of Department Psychological Medicine
The University of Auckland,
Private Bag 92019, Auckland 1142
Email: s.merry@auckland.ac.nz
Phone: +64 (0) 9 923 6981

For any queries regarding ethical concerns, contact the Chair, The University of Auckland Human Participants Ethics Committee, The University of Auckland, Office of the Vice Chancellor, Private Bag 92019, Auckland 1142. Telephone 09 373-7599 ext. 83711. Email: ro-ethics@auckland.ac.nz

Approved by the University of Auckland Human Participants Ethics Committee on 10/10/17 for three years.
Reference Number 019958

The Healing Power of Art

PARTICIPANT CONSENT FORM

This form will be stored for a period of 6 years.

Researchers: Mikaela Law, Gregory Minissale, Elizabeth Broadbent and Tony Lambert

- I have read the Participant Information Sheet, and have understood the nature of the research.
- I understand that participation in this study is voluntary and will take me approximately 90 minutes to complete.
- I know that I am able to withdraw my participation at any time without giving an explanation and I can withdraw any data traceable up to one week after completing the study if I wish, in which case the data will be securely destroyed.
- I know who to contact if I have any questions about the study.
- I have had the opportunity to ask questions and have them answered to my satisfaction.
- I understand that my responses will be used for data analyses.
- I understand that participation in the study is confidential and that no material which could potentially identify me will be used in any reports or shared with any individual or organisation.
- I am aware that as a result of taking part in this study I will be given a $40 Countdown voucher as koha for agreeing to take part in this research, irrespective of whether I complete the study.
- I understand that during the experiment I will be asked to undergo an interview procedure role playing for a job application.
- I understand that my salivary samples will be stored securely at the University of Auckland at -20 degrees Celsius and may be sent to Germany for analysis after which they will be disposed of.
- I understand that throughout the experiment, I will complete a series of questionnaires, which include answering questions about my mood, health behaviours and demographics
- I understand that during the experimental session, some of my responses will be video-recorded

- I understand that the research data (including questionnaires, eye-tracking data and saliva samples) will be stored securely in the University of Auckland, Department Of Psychological Medicine for six years, after which it will be destroyed by shredding/deleting according to whether it is hard copy or electronic.
- I am not aware of any reason why I should not participate in this research

I agree to take part in this research.

Signature……

Date……

☐ I wish to receive a summary of the research findings.

Please email me at: ……..

Approved by the University of Auckland Human Participants Ethics Committee on 10/10/17 for three years. Reference Number 019958

Baseline Questionnaire

This questionnaire is designed to gather some background information on your demographics, as well as your feelings and mood. All of the information you give us is confidential to the researchers and will only be used for the purposes of the study.

For all these questions there are no right or wrong answers- an answer is correct if it is true for you. We are most interested in your own opinion. Please choose the response that best fits with your circumstances.

Thank you for your help with this study

Demographics Questionnaire

Please answer the following questions by filling in the blanks or ticking the circles that best correspond to you

22. What is your gender?
    - O Female
    - O Male
    - O Non-Binary/Other

23. How old are you? _____

24. Height _____cm

25. Weight _____kg

26. What ethnic group do you belong to? (check all that apply)
    - O New Zealand European/Pakeha
    - O Maori
    - O Samoan
    - O Cook Island Maori
    - O Tongan
    - O Chinese
    - O Indian
    - O Other: Please Specify _____

27. What is your highest level of completed education?
    - O Secondary school (up to and including year 11)
    - O Secondary school (including years 12 and 13)
    - O Technical or trade certificate
    - O University or polytechnic diploma
    - O Undergraduate University degree (e.g. Bachelor's degree)
    - O Postgraduate University degree- Honours
    - O Postgraduate University degree- Masters or PhD
    - O None of the above

28. What is your current employment status?
    - O Employed full time (40 or more hours per week)
    - O Employed part time (up to 39 hours per week)
    - O Student
    - O Not currently employed

Health- Related Behaviours

33. During the past three months how often have you drunk alcohol, on average?
    - O Not at all
    - O Less than once a month
    - O 1-3 times a month
    - O 1-2 times a week
    - O 3-6 times a week
    - O Every day

34. On the days when you did drink alcohol in the last three months, how many drinks did you have on an average day?
    - O 1-2 drinks
    - O 3-4 drinks
    - O 5-6 drinks
    - O 7-10 drinks
    - O 11 or more drinks
    - O N/A

35. During your average week, how many days do you engage in 30 minutes or more of physical activity (e.g. going for a walk or run, going to the gym, swimming)?
    - O Never
    - O 1 day
    - O 2 days
    - O 3 days
    - O 4 days
    - O 5 days
    - O 6 days
    - O Every day

36. During the past week, how would you rate your diet?
    - O Very poor
    - O Poor
    - O Fair
    - O Good
    - O Very good

37. Do you currently smoke?
    - O Yes. On an average day I smoke _____ cigarettes
    - O No, not anymore. I quit smoking _____ ago
    - O No, I have never smoked

38. Are you currently on any regular medication Yes/No
    If yes, please indicate the name of the medication(s)

    _____
    _____
    _____

The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month.

39. During the past month, what time have you usually gone to bed at night?
    _____ O'Clock

40. During the past month, what time have you usually woken up in the morning?
    _____ O'Clock

41. During the past month, how many hours of actual sleep did you get per night? (this may be different than the number of hours you spent in bed)
    _____hours of sleep per night

42. During the past month, how long (in minutes) has it usually taken you to fall asleep each night?
    _____ minutes

43. During the past month, how often have you had trouble sleeping because you cannot get to sleep within 30 minutes?
    - O Not during the past month
    - O Less than once a week
    - O Once or twice a week
    - O Three or more times a week

44. During the past month, how would you rate your quality of sleep?
    - O Very bad
    - O Fairly bad
    - O Fairly good
    - O Very good

The following 2 questions are for females only

1. On what date was the first day of your most recent menstrual cycle?

_____

N/A

5. Are you currently using hormonal contraceptives? Yes / No

If yes, please indicate the name of the medication

_____

Over the last 2 weeks, how often have you been bothered by any of the following problems? Please circle the appropriate number

	Not at all	**Several days**	**More than half the days**	**Nearly every day**
1- Little interest or pleasure in doing things	0	1	2	3
2- Feeling down, depressed or hopeless	0	1	2	3
3- Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4- Feeling tired or having little energy	0	1	2	3
5- Poor appetite or overeating	0	1	2	3
6- Feeling bad about yourself- or that you are a failure, or have let yourself or your family down	0	1	2	3
7- Trouble concentrating on things, such as reading or watching TV	0	1	2	3
8- Moving or speaking so slowly that other people could have noticed? Or the opposite; being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9- Thoughts that you would be better off dead or off hurting yourself in some way	0	1	2	3

If you checked off <u>any</u> of the 9 problems above, how <u>difficult</u> have these problems made it for you to do your work, take care of things at home, or get along with other people?

- O Not at all difficult
- O Somewhat difficult
- O Very difficult
- O Extremely difficult

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate how often you felt or thought a certain way by circling the appropriate number

	Never	Almost Never	Some-times	Fairly Often	Very Often
1- In the last month, how often have you been upset because of something that happened unexpectedly?	0	1	2	3	4
2- In the last month, how often have you felt that you were unable to control the important things in your life?	0	1	2	3	4
3- In the last month, how often have you felt nervous and "stressed"?	0	1	2	3	4
4- In the last month, how often have you felt confident about your ability to handle your personal problems?	0	1	2	3	4
5- In the last month, how often have you felt that things were going your way?	0	1	2	3	4
6- In the last month, how often have you found that you could not cope with all the things that you had to do?	0	1	2	3	4
7- In the last month, how often have you been able to control irritations in your life?	0	1	2	3	4
8- In the last month, how often have you felt that you were on top of things?	0	1	2	3	4
9- In the last month, how often have you been angered because of things that were outside of your control?	0	1	2	3	4
10- In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	0	1	2	3	4

Listed below are a number of statements. Please read each statement and then rate how much you agree that the statement describes how you are thinking <u>right now</u> by circling the appropriate number from 1 (strongly disagree) to 7 (strongly agree)

	Strongly Disagree			**Neutral**			**Strongly Agree**
1 Right now, I am conscious of my inner feelings.	1	2	3	4	5	6	7
2 Right now, I am reflective about my life.	1	2	3	4	5	6	7
3 Right now, I am aware of my innermost thoughts.	1	2	3	4	5	6	7
4 Right now, I am thinking about how happy or sad I feel.	1	2	3	4	5	6	7
5 Right now, I am thinking about the physical sensations I feel in my body.	1	2	3	4	5	6	7
6 Right now, I wonder why I react the way I do.	1	2	3	4	5	6	7
7 Right now, I am thinking about how tired or alert I feel.	1	2	3	4	5	6	7
8 Right now, I am thinking about the possible meaning of the way I feel.	1	2	3	4	5	6	7

Please rate whether you are currently experiencing any of the following symptoms by using the scale below. Read each symptom and then rate how much you are feeling that symptom right now by circling the appropriate number.

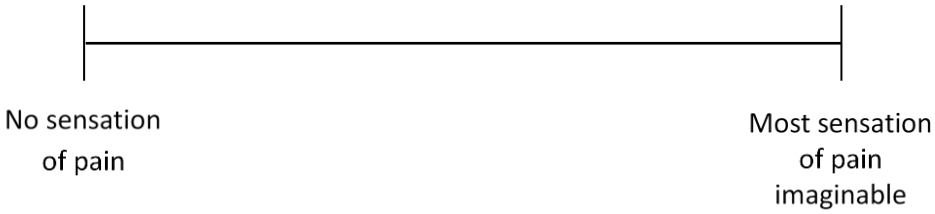
	Not Present	Mild	Moderate	Severe
Back or neck pain	0	1	2	3
Fatigue	0	1	2	3
Headache	0	1	2	3
Congested or runny nose	0	1	2	3
Joint pain or stiffness	0	1	2	3
Cough or sore throat	0	1	2	3
Upset stomach or indigestion	0	1	2	3
Muscle pain	0	1	2	3
Dry mouth	0	1	2	3
Drowsiness	0	1	2	3
Breathing problems	0	1	2	3
Numbness or tingling sensations	0	1	2	3
Abdominal pain	0	1	2	3
Muscle weakness	0	1	2	3
Dizziness	0	1	2	3
Nausea	0	1	2	3
Fever or increased temperature	0	1	2	3
Abnormal sweating	0	1	2	3

Listed below are a number of words that describe feelings. Some of the feelings are very similar to each other, whereas others are very different from each other. Read each word and then rate how much you feel that emotion right now by circling the appropriate number.

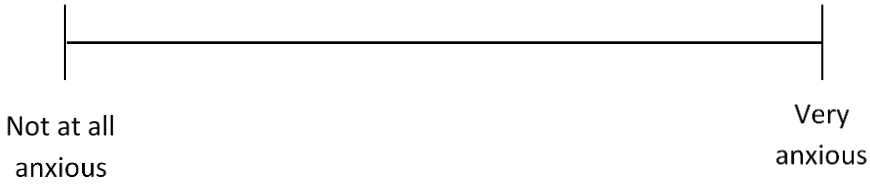
	Not at all	A little	Moderately	Quite a bit	Extremely
Still	1	2	3	4	5
Dull	1	2	3	4	5
Excited	1	2	3	4	5
Hostile	1	2	3	4	5
Strong	1	2	3	4	5
Sluggish	1	2	3	4	5
Aroused	1	2	3	4	5
Rested	1	2	3	4	5
Astonished	1	2	3	4	5
Quiet	1	2	3	4	5
Surprised	1	2	3	4	5
Enthusiastic	1	2	3	4	5
Passive	1	2	3	4	5
Fearful	1	2	3	4	5
Sad	1	2	3	4	5
Sleepy	1	2	3	4	5
Peaceful	1	2	3	4	5
Nervous	1	2	3	4	5
Relaxed	1	2	3	4	5
Lonely	1	2	3	4	5
Content	1	2	3	4	5
Calm	1	2	3	4	5
Happy	1	2	3	4	5
Unhappy	1	2	3	4	5
Satisfied	1	2	3	4	5

Please rate your current level of <u>stress</u> on the scale below by putting an X on the appropriate place on the line.

Please rate how much <u>pain</u> you are currently experiencing on the scale below by putting an X on the appropriate place on the line.



Please rate how <u>anxious</u> you currently feel on the scale below by putting an X on the appropriate place on the line.



Please rate how <u>relaxed</u> you currently feel on the scale below by putting an X on the appropriate place on the line.

Appendix E: TSST Instructions

TSST Script

It is very important that you listen to these instructions carefully. You will now participate in a speech task. The best speech in this study will win a $100 voucher so it is important to try and do a good job.

Do your best to imagine the following scenario is really happening to you:

You have applied for your dream job, and have to make a speech which will be video recorded for a panel of judges. You must convince this panel that you are the best candidate for your dream job. You will have 3 minutes to prepare your speech and then 5 minutes to present your speech.

I will be putting a video camera on the bed which will record your speech. You must look directly at the camera and speak for the full 5 minutes. If you stop, you will be encouraged to keep speaking until your time is up. The video recording will later be shown to the panel of judges who will rate your performance and I will also be rating your speech live.

Please ensure your speech covers:

- What is your dream job?
- Why do you want this job?
- Why you think you deserve it?

You will now have 3 minutes to prepare your speech.

Do you have any questions?

Your 3 minutes preparation time starts now.

Time for speech Script

Your 3 minutes preparation time is now done. You will now have 5 minutes to present your speech to the camera. Remember that you must speak for the entire 5 minutes and you must look directly into the camera. I will tell you when your 5 minutes is up.

Your 5 minutes speaking time starts now.