“Utilizing Virtual Reality as a therapeutic tool in Psychiatry”

by

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DECLARATION

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Date: April 2022 . . . . . .

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- Thank you to AxioVR (PTY) LTD for providing the laptop, 3D printer and VR headset used in the present project.
- For the sound effects royalty free sound content were licensed from **Audiojungle**.
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  - The **Industrial Kitbash and Coal Mine Set**.
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  - Environment meshes from the **Factory Environment Collection**
  - Selected environment meshes from the **Modular Warehouse** content pack.
- From Turbosquid: **Industrial Access Ladder 3D model by Root-Moos**.

DEDICATION

Vir Ben du Plessis, die siviele ingenieur : Sien nou Pa, ek bou nou ook brûe, maar van n ander aard.

ABSTRACT

The mass production of modern cellphone technology has resulted in a dramatic cost reduction of producing Virtual Reality (VR) head-mounted displays. Although VR has been effective in the treatment of phobias, uptake is still far from mainstream. Fear of heights (i.e. acrophobia) is one of the more common forms of phobias in the general population. Up to 28% of people have distress and anxiety when exposed to heights (i.e. visual heights intolerance (VHI)), with up to 6% of people meeting clinical criteria for the specific phobia. Virtual Reality Exposure Therapy (VRET) for acrophobia has been shown to be effective as early as the 1990s. There are, however, still relatively few randomized controlled studies that have looked at its effectiveness . Even fewer studies look at physiological responses associated with fear cessation. Biofeedback is the process of presenting participants with their physiological responses allowing them to gain a measure of control over them. Biofeedback shows promise as a treatment adjunct for specific phobias. We therefore aim to create a VR height exposure platform, that offers a graduated exposure, is optimized to avoid excessive motion sickness, is cost-effective for widespread use, and is validated by participant reports collected during the exposure.

Here we developed and tested a cost effective VR acrophobia environment with biofeedback in a sample of 22 participants, 4 of whom had clinically measurable acrophobia. We constructed an Electrodermal Activity (EDA) biofeedback prototype using two Arduino boards, one being electrically isolated (Nano) to reduce noise and increase safety. The second Arduino (UNO R3) was connected via USB to a VR workstation running the Unreal Engine 4.24.2. USB connectivity was established via the UE4duino plugin. All participants underwent clinical screening, excluding for confounding psychopathology except acrophobia. Acrophobia symptoms were evaluated using the Visual Height Intolerance Severity Scale (vHISS) questionnaire. Participants were placed on a VR platform which ascended to 28 meters. Subjective stress responses were

recorded during the task as well as VR related motion sickness. Data was entered into a repeated measures ANOVA to check for within-subject differences in levels of stress, comparing when the platform was on the ground as well as in the air. Afterwards participants experiences were evaluated via a brief questionnaire.

Biofeedback based on the mean of the signal consistently informed participants that they were stressed while the platform was elevated. Participants showed a significant increase in mean skin conductance signal while the platform was elevated. Continuous decomposition analysis as well as subjective responses confirmed the accuracy of the biofeedback provided. All participants reported a positive experience using the biofeedback, most perceiving it to be accurate.

The present work indicates that biofeedback in VRET is a promising treatment adjunct, which should be explored in further clinical trials.

Key words:

Electrodermal Activity; VRET; Acrophobia

OPSOMMING

Met die koms van die massaproduksie van die moderne selfoontegnologie, het die koste van die vervaardiging van Virtual Reality (VR) kopgemonteerde skerms gedaal. Alhoewel VR baie belowend is met die behandeling van akrofobie, vrees vir vlieg en ander, is die opname nog ver van die hoofstroom. Hoogtevrees (d.w.s. akrofobie) is een van die meer algemene vorme van fobies in die algemene bevolking. Tot 28% van mense ervaar nood en angs wanneer hulle aan hoogtes blootgestel word (d.i. visuele hoogte-intoleransie (VHI)), met tot 6% van mense wat aan kliniese kriteria vir die spesifieke fobie voldoen. VRET vir akrofobie is reeds in die 1990's doeltreffend getoon. Daar is egter nog relatief min gekontroleerde studies wat na die doeltreffendheid daarvan gekyk het. Nog minder wat kyk na fisiologiese reaksies wat verband hou met vreesbeëindiging. Bioterugvoer is die proses om deelnemers hul fisiologiese reaksies voor te stel wat hulle in staat stel om 'n mate van beheer oor hul fisiologie te verkry. Bioterugvoer blyk belowend as 'n behandelingsaanvulling vir spesifieke fobies. Ons beoog dus om 'n VR-vrees vir hoogte-blootstellingsplatform te skep, wat geleidelike blootstelling bied, geoptimaliseer is om oormatige bewegingsiekte te vermy, koste-effektief is vir wydverspreide gebruik en bekragtig word deur kliëntverslae wat ingesamel word tydens die blootstelling.

Hier het ons 'n koste-effektiewe VR-akrofobie-omgewing met bioterugvoer ontwikkel en getoets in 'n gesonde steekproef van 22 deelnemers, van wie 4 kliniies meetbare akrofobie gehad het. Ons het 'n Electrodermal Activity (EDA) bioterugvoer toestel gebou deur van twee Arduino-borde gebruik te maak, waarvan een elektries geïsoleer is (Nano) om die sein te verbeter en veiligheid te verhoog. Die tweede Arduino (UNO R3) is via USB gekoppel aan 'n VR-werkstasie met die Unreal Engine 4.24.2. USB-verbinding is tot stand gebring deur die UE4duino-plugin. Alle deelnemers het kliniese sifting ondergaan, en is uitgesluit vir psigopatologie behalwe akrofobie. Akrofobie simptome is geëvalueer deur gebruik te maak van die Visual Height Intolerance Severity Scale

(vHISS) vraelys. Deelnemers is op 'n VR-platform geplaas wat tot 28 meter gehys is. Subjektiewe stresreaksies is aangeteken tydens die taak sowel as VR-verwante bewegingsiekte. Data is in 'n repeated measures ANOVA ingevoer om te kyk vir *within-group* verskille in stresvlakke, met vergelyking wanneer die platform op die grond sowel as in die lug was. Daarna is deelnemers se ervarings deur middel van 'n kort vraelys geëvalueer.

Bioterugvoer gebaseer op die gemiddelde van die sein het deelnemers konsekwent ingelig dat hulle gestres is terwyl die platform in die lug was. Deelnemers het 'n beduidende toename in gemiddelde velgeleidingsein getoon terwyl die platform verhewe was. 'n *Continuous decomposition analysis*, sowel as subjektiewe response het die akkuraatheid van die bioterugvoer bevestig. Alle deelnemers het 'n positiewe ervaring met die gebruik van die bioterugvoer gerapporteer, en die meeste het dit as akkuraat beskou.

Die huidige werk dui aan dat bioterugvoer in VRET 'n belowende behandelingshulpmiddel is, wat in verdere kliniese proewe ondersoek moet word.

Sleutelwoorde:

Elektrodermiese aktiwiteit; VRET; Akrofobia

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LIST OF ABBREVIATIONS AND/OR ACRONYMS

VR Virtual Reality 2

HMD Head Mounted Display 2

GPU Graphical Processing Unit 2

PTSD Post Traumatic Stress Disorder 3

VRET Virtual Reality Exposure Therapy 3

EDA Electrodermal Activity 5

SC Skin Conductance 10

SR Skin Resistance 12

G Conductance 12

SCR Skin Conductance Response 13

TTP Trough-To-Peak 13

SCL Skin Conductance Level 14

NS.SCR Nonspecific Skin Conductance Response 14

CDA Continuous Deconvolution Activity 15

ADC Analog-to-Digital Converter 20

DAC Digital-to-Analog Converter 22

vHISS Visual Height Intolerance Severity Scale 25

HIQ Heights Interpretation Questionnaire 34

CHAPTER 1

INTRODUCTION

Virtual Reality (Virtual Reality (Virtual Reality (VR))), the immersion of a user in an artificial environment by means of a head-mounted display (Head Mounted Display (Head Mounted Display (HMD))), was first introduced in the 1950's (VRH, 2019). The mass production of modern cellphone technology significantly reduced the cost of producing VR head-mounted displays. This cost reduction is due to the shared hardware dependencies, for example motion tracking, between VR and cellphones (Ocu, 2014). A pivotal limitation of older VR HMDs was the common occurrence of motion sickness among users (Kim *et al.*, 2021). Motion sickness is thought to result when there is a delay between the VR display and the position sense of the vestibularcochlear system. Modern graphic rendering capabilities common among even the mobile platforms, such as the Oculus Quest, has virtually erased the occurrence of motion-sickness, which can easily compensate for rapid changes in users' direction (Ocu, 2014).

The use of VR as a psychotherapeutic tool began in the 1990's (VRH, 2019). Older systems were primitive compared to modern VR environments. Although VR has been effective in the treatment of phobias, for example fear of flying and fear of heights(Opris *et al.*, 2011), uptake is still far from mainstream (Neudeck and Wittchen, 2012). Recently companies such as Psious have made advances in bringing VR therapy to the psychotherapy office with cost effective offerings. Nevertheless, given the rapid advances of the technology not just in HMDs and Graphics Processing Units (Graphical Processing Unit (GPU)), but in the availability of easy to configure microcontrollers such as the Arduino, the potential of VR therapeutic offerings are still likely unplumbed.

One particular clinical area where VR has shown the greatest promise, is exposure therapy (Opris *et al.*, 2011). Exposure therapy has proven to be one

of the most effective and empirically verified treatment options in psychology (Wechsler *et al.*, 2019). Exposure therapy involves exposure to a particularly feared environment (e.g. small spaces), animal (e.g. spiders) or context (e.g. public speaking), allowing cognitive and emotional adaption to occur, resulting in the sustained reduction of fear. It is particularly effective in the treatment of fear and anxiety disorders, as well as Post Traumatic Stress Disorder (Post Traumatic Stress Disorder (PTSD)) (Wechsler *et al.*, 2019). Effects of exposure therapy has also been shown to be stable over time (Wechsler *et al.*, 2019).

1.1 PROJECT MOTIVATION

Fear of heights (i.e. acrophobia) is one of the more common forms of phobias in the general population. Up to 28 % of people experience distress and anxiety when exposed to heights (i.e. visual heights intolerance (VHI)), with up to 6% of people meeting clinical criteria for a specific phobia (i.e. acrophobia) (Huppert *et al.*, 2020). Virtual Reality Exposure Therapy (Virtual Reality Exposure Therapy (VRET)) for acrophobia has been shown to be effective as early as the 1990s (Rothbaum *et al.*, 1995). There are, however, still relatively few randomized controlled studies that have looked at its effectiveness (Carl *et al.*, 2019). Even fewer that looks at physiological responses associated with fear extinction (Witte *et al.*, 2019).

VR based exposure as well as exposure therapy in general is often criticised as not being interactive enough, being "done-to" the patient rather than done "with" the patient (Neudeck and Wittchen, 2012). Although patients' stress responses are often monitored by the therapist (i.e. physiological feedback), patients are rarely made directly aware of these elevated responses (i.e. biofeedback). Exposure-based therapy relies on providing challenging levels of stress without being overwhelming to be effective. As of this writing biofeedback shows promise, but few studies have looked into its utilization in VR and none that we are aware of in acrophobia. As physiological responses gathered during

treatment do not necessarily represent fear responses of a patient, but general arousal, biofeedback needs to be cross-validated with the subjective reports of the patient, as well as a clinical assessment by an experienced clinician.

Although proven to be effective, widespread use of exposure therapy in treatment faces several challenges. Often clinicians are worried that overwhelming exposure might lead to severe distress and actual harm in their patients (Neudeck and Wittchen, 2012). A slow and graduated exposure is therefore necessary. The additional cost of a VR HMD and a GPU capable of driving the HMD could potentially be prohibitive in lower resourced settings due to the cost involved.

1.2 PROBLEM STATEMENT

VR based exposure therapy has been shown to be as effective as *in vivo* exposure (Opris *et al.*, 2011), making this a promising treatment alternative. There are, however, several factors that hinder its widespread adoption. Firstly, exposure based therapy often lacks direct patient participation, being largely driven by the therapist. Secondly, over-exposure and motion sickness is difficult to control *in vivo*. Thirdly, for the environment to be rendered in a realistic way, VR platforms are often not cost-effective. Lastly, to allow both the patient as well as the therapist to select an optimal exposure level, the use of biofeedback should be investigated and validated.

We therefore aim to create a cost effective VR height exposure environment, that offers a graduated exposure, is optimized to avoid excessive motion sickness, is cost effective for widespread use and is validated by patient reports collected while the exposure is ongoing.

1.3 AIMS AND OBJECTIVES

Primary Aim: Create a VRET environment that provides an interactive and immersive experience, which can facilitate exposure therapy in a lower to middle income context.

Objectives: Create and test a height exposure VR according to the following parameters:

- Allows for user feedback while immersed in VR in terms of tolerability (i.e. nausea and fear level) and safety (i.e. Panic button).
- Optimize the environment to run with minimal motion sickness related side effects.
- Utilize a cost effective VR platform
- Construct an Electrodermal Activity (Electrodermal Activity (EDA)) biofeedback prototype unit based on a cost effective platform.
- Provide visual biofeedback of the participant's EDA response to assist in patient comprehension and cognitive adjustment.
- Validate Biofeedback responses by comparing them to subjective responses collected while participants were immersed in the VR environment.

CHAPTER 2

LITERATURE REVIEW

2.1 EXPOSURE THERAPY

A number of theories have been proposed that seek to account for the effectiveness of exposure therapy. In the late 1950s exposure therapy was conceptualized as a method of increasing the levels of relaxation in patients (i.e. reciprocal inhibition) (Wolpe, 1954). These increased levels of relaxation were thought to counteract anxiety provoked by threatening stimuli. This theory did not receive good empirical support, as patients improved regardless of their levels of relaxation when asked to evoke stressors consciously in their mind (McGlynn *et al.*, 1979). Interestingly enough, increasing levels of relaxation did indeed prove to be effective in some cases, but only when it was associated with increased levels of autonomic arousal (Levin and Gross, 1985). This increased response is thought to be similar to that observed in exposure to aversive stimuli. This would suggest that exposure requires at the very least, an engagement of the autonomic nervous system, a crucial component of the fear response. Subsequently, the emotional processing theory postulated that the autonomic nervous system, and by implication the fear response, is habituated after repeated exposure to the threatening stimulus (Foa and Kozak, 1986). Central to this theory was that habituation preceded a necessary cognitive correction. That is, as the nervous system is attenuated, it is followed by a rational (i.e. cognitive) insight that the patient's emotional response was indeed exaggerated relative to the fearful stimulus. This insight would then drive recovery. The emotional processing theory, although very influential, received inconsistent support. Mainly, the level of habituation and even the between session reductions in fear did not prove to be the key factor in ultimate treatment success (Craske *et al.*, 2008). This resulted in an increased emphasis placed on cognitive correction strategies, without depending on fear habituation.

Currently fear extinction is still seen as a driving force in the treatment success seen in exposure therapy (Craske *et al.*, 2012). It has generally thought to have both an emotional arousal component as well as a cognitive component. As a result, the most important theoretical framework for exposure therapy has proven to lie in the field of extinction-based learning (Craske *et al.*, 2008). Within the field of neurobiology, learning is thought to result in a set of predictions specifying distinct outcomes based on specific environmental cues (i.e. "a stimulus") (Morrison and Ressler, 2014). The more a stimulus is matched with a specific outcome temporally, for example leaves rustling followed by a predator pouncing, the stronger the prediction will be associated with this specific outcome (Morrison and Ressler, 2014). In this example the rustling of leaves would result in a strong fear response, which would drive an autonomic flight response, for example. This includes elevated heart-rate, higher breathing rate, increased central nervous system arousal and an emotional fear response, all helping the animal escape the predator. Although crucial for the survival in animals and in humans, this form of learning is directly implicated both in anxiety disorders as well as post-traumatic stress disorder (Norrholm and Jovanovic, 2018). An exaggerated fear response could paralyze an organism, rendering them vulnerable to predators. Moreover, a strong stimulus response often generalizes to closely associated stimuli and stimulus contexts (Andreatta *et al.*, 2017). To continue our present example, a fear response to "leaves rustling" can often generalize to most unknown audible sounds (i.e. closely associated stimuli), even in environments considered safe (i.e. similar contexts). This is especially important in humans, as it could lead to a frequently aroused physiological state accompanied by fear, which is the core feature of most anxiety disorders and PTSD (O'Shea, 2009). These disorders are commonly associated with other co-morbid disorders such as depression and substance abuse (O'Shea, 2009). Importantly, fear extinction learning is conceptualized as the opposite of stimulus-outcome pairing (Morrison and Ressler, 2014). It is the process where in the repeated absence of an outcome

associated with a particular stimulus, the paring is ultimately undone (Morrison and Ressler, 2014). In our previous example, given enough time where "leaves rustling" is not followed by the appearance of a predator, ultimately the animal learns not to respond with a strong fight or flight response to conserve resources (i.e. fear extinction) (Morrison and Ressler, 2014). Currently exposure therapy is thought to undo pathological learned fear-responses, by repeated exposure to a fear-inducing stimulus in the absence of an adverse outcome (Morrison and Ressler, 2014).

Although well established, exposure therapy still has limitations. For example, it is still uncertain what the relative contribution is of the cognitive adjustment or the emotional arousal/extinction component (McMillan and Lee, 2010). This is mainly due to an overabundance of variables that are hard to control in a classic experimental environment (Rosen and Davison, 2003). In the case of acrophobia, this includes the difficulty of manipulating the height parameter in a real-world environment, as well as taking safety considerations into account. Patient participation is often lacking, leading to exposure therapy being criticized of being done "to" a patient and not done "with", impeding the development of a positive cognitive framework (Cook *et al.*, 2005). Such practical difficulties in exposing patients to aversive stimuli make it difficult to maintain an appropriate level of stimulation, potentially leading to either excessive or even under exposure. Often clinicians avoid exposure therapy for this reason, despite its efficacy, as it is seen as potentially worse than the symptoms experienced by the patient (Cook *et al.*, 2005). This has been disproved, however, as many patients report high levels of confidence in exposure therapy, citing that adverse events, such as panic attacks and dizziness, are considered common place for those suffering from these disorders (O'Shea, 2009), and occur in a controlled environment in the presence of a therapist (Deacon and Abramowitz, 2005).

Several lines of inquiry have been explored in recent years to address these

concerns. Practical methods, such as scaling a tall building with a patient, although effective, could potentially fall out of favor. Currently advances in VRET occur alongside the rapid development of virtual reality display technologies (Chesham *et al.*, 2018). VRET addresses issues of safety and has proven to be potentially just as effective in the treatment of anxiety disorders as treatment as usual. In recent years VRET reliably induces anxiety in participants as well as results in fear extinction. VRET has been found to be equally effective compared to Cognitive Behavioral Therapy (Chesham *et al.*, 2018), another gold standard treatment in anxiety. Preliminary evidence suggest that resultant fear extinction in the virtual environment is not limited to the virtual environment alone, but is likely to remain after the session. This can lead to decreased levels of fear in real life (i.e. non-virtual) scenarios, facilitating further in vivo exposure (Opris *et al.*, 2011). Although active, the development of virtual reality exposure-based therapy tools is still in its infancy. Few if any tools address participant engagement to help facilitate cognitive adjustments (Opris *et al.*, 2011).

Although tools do offer gradual exposure to a stimulus, it still has not realised its full potential. Current Virtual Reality environments also need to explore what the hardware is capable of delivering, while remaining cost effective and tolerable. Borderline hardware performance can result in a mismatch between the visuals that are being rendered at any given moment, and the position of the head. This often results in nausea and dizziness. This could theoretically result in a stress response unrelated to the fear cue being presented, which could result in suboptimal exposure. It could also result in the patient terminating the treatment altogether.

2.2 MEASURING STRESS RESPONSES

2.2.1 The Autonomic nervous system

The nervous system can be divided generally into central and peripheral components. As mentioned, our present measures of physiological arousal (i.e. heart-rate variability and electrodermal activity) are made possible by the activity of the autonomic nervous system (Boucsein, 2012), a sub-component of the peripheral nervous system. The autonomic nervous system consists of the parasympathetic and sympathetic system. The parasympathetic system is regulates bodily functions associated with recuperation during periods of relaxation. In contrast, the sympathetic system is associated with the flight or fight response, during periods of heightened threat for example. Activity of the sympathetic nervous system is of particular interest in exposure therapy, as decreasing threat related activity associated with successful treatment (Morrison and Ressler, 2014).

2.2.2 Electrodermal activity

2.2.2.1 The central origin of electrodermal activity

Electrodermal activity arises from variable water content in sweat glands, which in turn alters the conductive properties of the skin (i.e. Skin Conductance (Skin Conductance (SC)))(Boucsein, 2012). It is known that EDA originates as activity in the central nervous system and not just as a result of mere thermoregulatory phenomena (See Figure 2.1). Interestingly, the innervation at certain sites, notably the palms and plantar sections of the feet, are almost exclusively sympathetic (Boucsein *et al.*, 2012). Early studies performed in cats and primates also demonstrated that sympathetic activity associated with EDA responses likely have their origin in higher cortical and limbic regions. Electrical stimulation of cortical regions, would result in electrodermal responses in the cat's fat pads for example (Sequeira and Roy,

1993). In monkeys, ablation of the frontal cortex would result in impaired EDA responses following acoustical startle probes (Kimble *et al.*, 1965). Recent functional magnetic resonance imaging have confirmed this association in humans *in vivo*, showing an association between EDA responses and amygdala and medial-frontal cortical activity (Williams *et al.*, 2001). These results demonstrate that EDA activity can serve as an objective measure of human arousal status. Although, theoretically, as any state of arousal could result in an EDA response, specific emotions such as fear and anxiety would still need to be cross-validated by other means. This includes subjective reports by the participant as well as clinical correlates (Boucsein *et al.*, 2012).

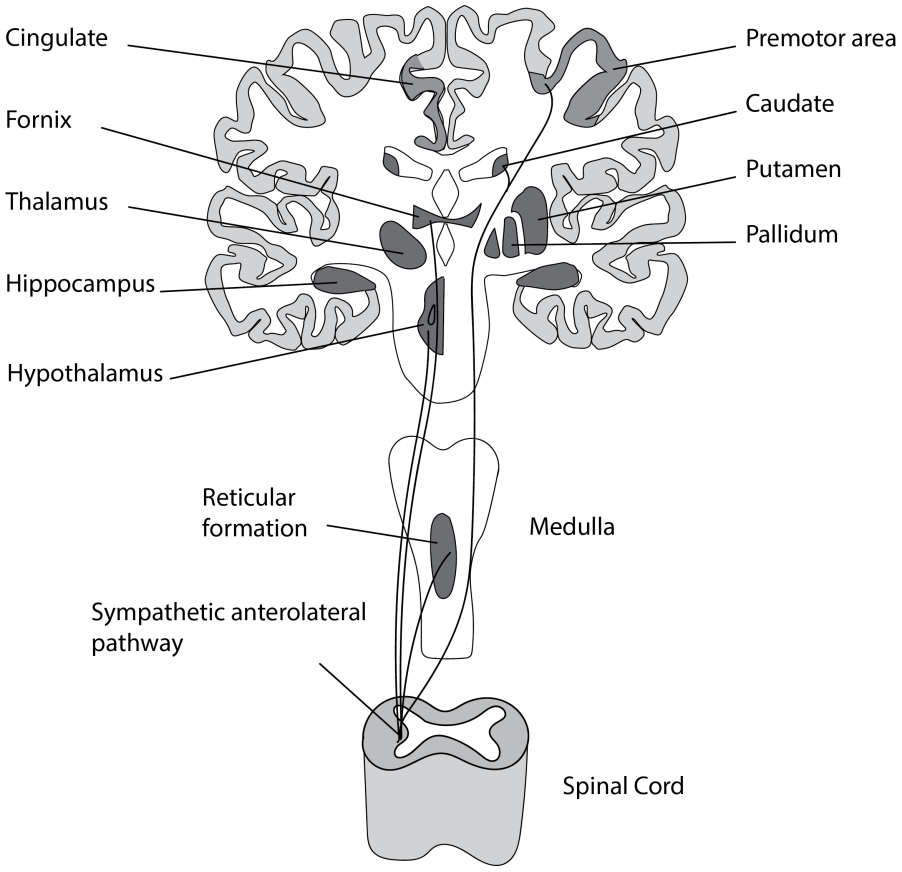


Figure 2.1: The central origin of the EDA signal.

2.2.2.2 Measuring electrodermal activity

Electrodermal activity has been used to monitor physiological arousal was around since the 1880's ((Posada-Quintero and Chon, 2020)). Established methods and nomenclature was established in the 1960's and 70's, with little differences in basic measurement technique since this time in the latest publication recommendations ((Posada-Quintero and Chon, 2020)). The two main types of measurement are *endosomatic* and *exosomatic*. *Endosomatic* methods rely on the direct measurement of potential differences on the skin itself, while *exosomatic* techniques involve applying a current over the skin. When the current is kept constant and voltage differences are measured, skin resistance measurements are collected (Skin Resistance (SR)), while skin conductance (SC) measures are obtained when the voltage is kept at a constant (a.k.a *quasi-constant voltage method*) (Boucsein *et al.*, 2012). It is common practice to convert SR measurements into SC measurements, with conductance (Conductance (G)) being the reciprocal of resistance.

$$G = 1/R \tag{2.1}$$

Given that resistances in biological processes commonly range in thousands of Ohm, skin conductance is commonly measured in microsiemens (μS) (Boucsein *et al.*, 2012). Converting a kilo-ohm resistance value to microsiemens is done in the following way:

$$G[\mu\text{S}] = \frac{1,000}{R[\text{k}\Omega]} \tag{2.2}$$

Here we refer to our electrodermal measurements as "EDA" as this umbrella term encompasses both SR and SC methods (Boucsein *et al.*, 2012).

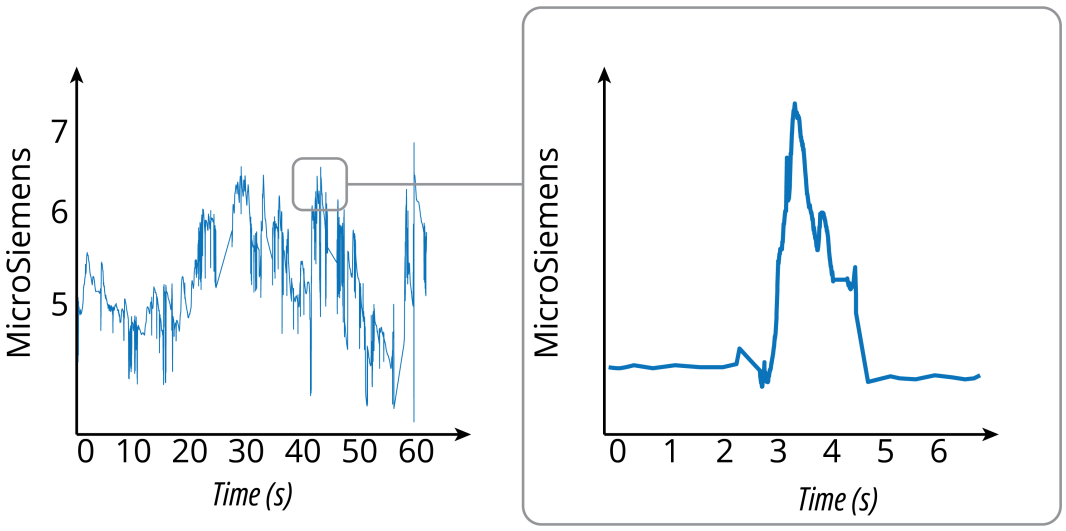


Figure 2.2: The tonic and phasic components of the EDA signal

2.2.2.3 Important aspects of the electrodermal signal

Two important aspects of the EDA signal are the tonic as well as the phasic components (See Figure 2.2). They are related, but can represent different aspects of subject arousal (Boucsein *et al.*, 2012). The tonic component consist of the relatively slowly changing mean signal. This indicates a more general arousal level.

In contrast, the phasic component consists of rapid changes in signal, typically 1 to 5 s after a specific stimulus (i.e. loud noise burst, breath holding etc.). The signal usually peaks at around 0.5 to 5 seconds, after the initial rise for a minimum of 0.05 down to 0.01 μS (See Figure 2.3).

The established approach to determining the Skin Conductance Response (Skin Conductance Response (SCR)) peaks by means of directly scoring according to peak timing and rise times according to these parameters is referred to as a Trough-To-Peak (Trough-To-Peak (TTP)) analysis, which represents the established approach generally taken (Boucsein, 2012). Evaluating for phasic spikes in the EDA signal is more important in behavioural experiments with event related stimuli, i.e. stimuli that happen at specific points in time (Boucsein *et al.*, 2012). As a consequence, studies that relay on event re-

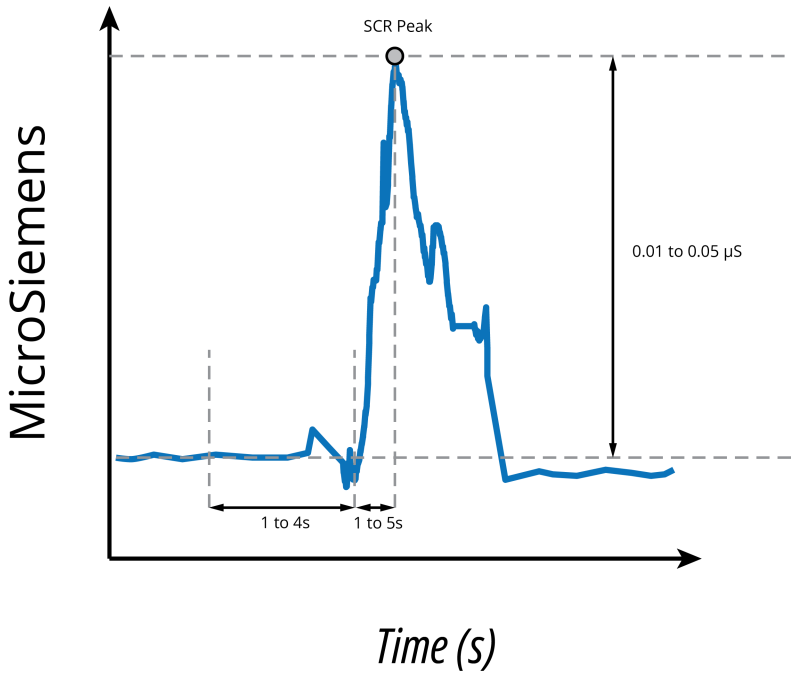


Figure 2.3: Individual skin conductance response definition

lated timings, often require a high temporal resolution (i.e. 200 Hz+) (Gersak, 2020).

In contrast, studies that examine stimuli that occur over longer continuous periods of time, rely more on the tonic component, referred to as the Skin Conductance Level (Skin Conductance Level (SCL)). Importantly, determination of SCR peaks are still valuable for such experiments, but here the number of occurrences of nonspecific Skin Conductance Responses over an exposure period (Nonspecific Skin Conductance Response (NS.SCR)) are used to help estimate the SCL. Commonly SCRs are evaluated and subtracted from the signal, as the raw EDA signal contains both components (See Figure 2.2) (Gersak, 2020). For brevity we will refer to all skin conductance responses as SCRs in the present manuscript, it should be noted that as we do not intend to use a strict event related design, all SCRs are strictly speaking NS.SCRs. Furthermore, it would be more accurate to refer only to an estimate as an "SCL" once the SCR component is removed. We will therefore differentiate by calling the non-deconvolved SCL as the "raw" EDA measure.

In general, SCRs often overlap, which marks a limitation in the classic TTP approach. Recently newer deconvolution methods have been developed to address this limitation (Alexander *et al.*, 2005). These methods assume that postganglionic sudomotor fibers (See Figure 2.4) cause a positive inflection on the signal when the sweat glands are activated. Using a non-negative deconvultion method therefore accounts for overlapping SCRs, while examining specific positive driver thought to be associated with sudomotor nerve activity. This Continuous Deconvolution Activity method (Continuous Deconvolution Activity (CDA)) splits the EDA raw signal into SCL and SCR components. Here we refer to SCRs derived from this method as CDA responses, to distinguish it from the classical TTP method (Benedek and Kaernbach, 2010).

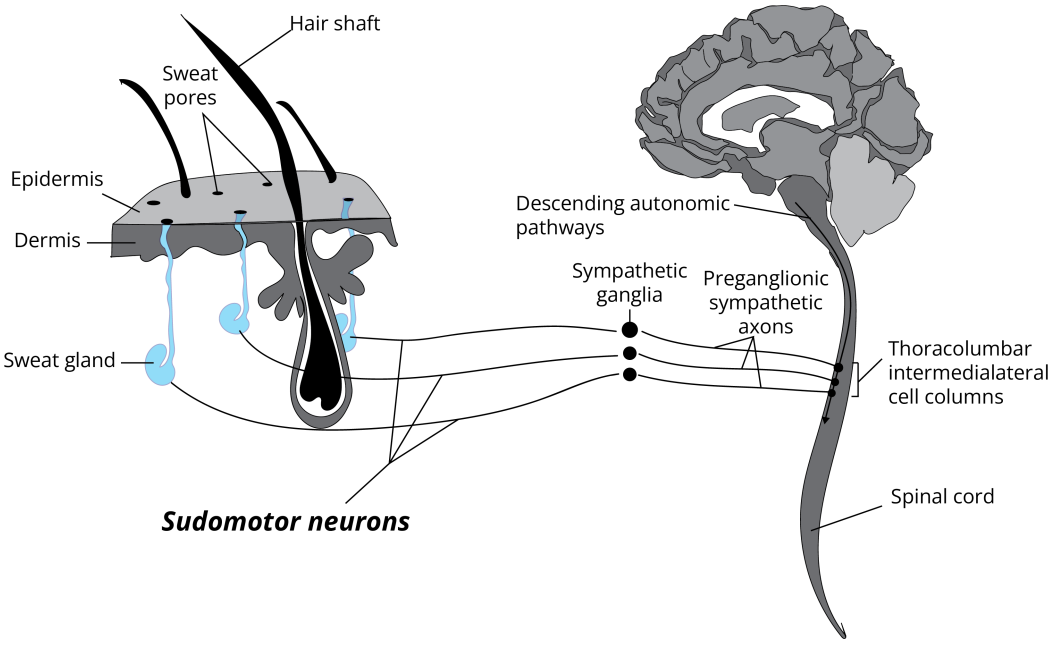


Figure 2.4: Sudomotor Fibers

2.2.2.4 Important considerations in the measurement of EDA

There are several important factors to keep in mind when measuring EDA levels. The stratum corneum is constantly kept in a hydrated state, as there is a constant flow of water from the dermis via the epidermis via insensible perspiration (Boucsein *et al.*, 2012). An important assumption is that this hydrated

state stays constant while changes in conductance is mostly related to changes in the sweat gland ducts as they activate according to sympathetic nervous system tonus (Boucsein, 2012). Factors that can influence the skin's water content are therefore crucial to regulate experimentally. Firstly, ambient temperature and humidity should be kept in normal ranges to avoid fluctuations in skin temperature that could influence the base line water content. The electrolyte concentration of sweat can also influence skin hydration. It remains controversial however, to what extent the palmar and plantar surfaces contribute to thermoregulatory sweating (Boucsein *et al.*, 2012). Secondly, electrolyte concentration in the electrode conductive material used (i.e. electrode gel/paste) could also disturb the resting water content of the skin (Dormire and Carpenter, 2002). It is advised that usually the electrodes should be as isotonic as possible (Boucsein *et al.*, 2012). Challenges in electrode adherence as well as viscous properties of the media often result in a trade-off between good-electrode adherence, its conductive properties and negative impact on skin conduction.

In *exosomatic* recordings, the voltage and current applied over the fingers should also be considered. Lower currents result in smaller recorded signal fluctuations, which could require additional amplification. Larger currents could result in paralysis of the sweat glands, and in extreme cases damage to the ducts themselves(Lykken and Venables, 1971). Applied voltages are standardized to 1 volts (Boucsein *et al.*, 2012). However, values between 1 to 4 volts are still considered to be low voltage manipulations (Chizmadzhev *et al.*, 1998). Higher voltages are safely used in transcutaneous DC stimulation, where 2 mA currents are applied for up to 22 minutes using various size electrodes, with high voltages (60 volts +) with no ill effect (Minhas *et al.*, 2010).

Originally scrolling paper reels were used for recording EDA measurements (Boucsein *et al.*, 2012). For modern applications, a 16-bit Analogue to Digital Converter allows for a 0.0015 μS recording resolution, and is sufficient to cap-

ture the minimum 0.05 μS elevations of EDA signals (Boucsein *et al.*, 2012). The sampling rate of the signal acquisitions needs to be greater than 10 Hz to capture the 0.5 to 5 second time windows in which SCR signals occur (Gersak, 2020).

2.3 BIOFEEDBACK IN CLINICAL PRACTICE

Biofeedback is the practice of making real-time physiological measures available to patients, allowing them to gain control of the underlying physiological process (Dillon *et al.*, 2016). Biofeedback has been associated with decreased levels of physiological arousal when compared to control conditions such as sham feedback (Dillon *et al.*, 2016). Biofeedback is a promising treatment adjunct in anxiety disorders, where it is often difficult for patients to monitor their own stress levels, by providing additional insight allowing them to recognize and alter maladaptive cognitive and emotional responses (Schoenberg and David, 2014). Despite the well-established nature of EDA measurement, little work has been done exploring the use of biofeedback using EDA in stress and anxiety. In a review of all biofeedback studies done between 1976 and 2014, only 4.8% (n=3) used EDA based biofeedback (Schoenberg and David, 2014). These three studies reported some effectiveness of EDA based biofeedback in the treatment of anoxrexia nervosa (Pop-Jordanova, 2000), depersonalization disorder (Schoenberg *et al.*, 2012) as well as anxiety reduction in highly anxious females (Khanna *et al.*, 2007). However, these studies did have some limitations such as a lack of a statistical analysis of clinical changes (Pop-Jordanova, 2000), abscence of a DSM-V diagnosable stress disorder (Khanna *et al.*, 2007) or could not replicated their findings in a randomized controlled trial (Schoenberg *et al.*, 2012).

In a recent systematic review of the combination of biofeedback and stress management, only 14 high quality studies were identified using the PICO-TS model for study bias detection (Witte *et al.*, 2019). Of them, only 2 used EDA

as the feedback method (Witte *et al.*, 2019). The first study demonstrated non-specific stress feedback training to be effective in reducing anxiety associated with food related cues (Teufel *et al.*, 2013). A second study examined the effectiveness of smartphone based biofeedback. They showed heart-rate based reductions for a biofeedback vs a non-biofeedback smartphone game(Dillon *et al.*, 2016). Although measures of heart-rate as well as heart-rate variability have been shown to to be useful as a biofeedback measure (Witte *et al.*, 2019), heart-rate based measures do not seem to be as effective in VR as in *in vivo*, as many studies report EDA to be a more sensitive measure, specifically for acrophobia (Norrholm and Jovanovic, 2018).

2.4 ACROPHOBIA

Surprisingly, given the aforementioned prevalence of visual heights intolerance (28% of the general population of which 50% needs therapy) as well as acrophobia (3-6% of the general population), there are no studies using biofeedback for the treatment of anxiety related to heights (Witte *et al.*, 2019).

Acrophobia is the excessive and persistent fear of heights (American Psychiatric Association, 2013). If left untreated, acrophobia has a chronic and unfavourable course of the illness. Acrophobia is often accompanied by major depression, chronic fatigue, panic attacks, social phobia and other specific phobias (Kapfhammer *et al.*, 2016). Main symptoms experienced by individuals with both visual heights intolerance and acrophobia include anxiety, vertigo and gait insecurity. (For a more complete list see Table 3.2, page 25). A coping strategy for affected individuals is often to avoid triggering situations, leading to restrictions in daily activities as well as a reduced quality of life. The spectrum of distressing stimuli often increases in more than half of affected individuals (Huppert *et al.*, 2013).

2.5 CONCLUSION

Taken together, there remains a lack of good studies examining the efficacy of biofeedback as a treatment adjunct in acrophobia as well as in VRET in general. We could find no studies examining the utility of biofeedback methods in VR. The present work aims to explore the use of biofeedback in VR in stress and anxiety, with a height exposure paradigm. Acrophobia is relatively straightforward to measure clinically, has a need for intervention in the general public (Huppert *et al.*, 2020) and has the possibility of creating an environment that can offer a graduated exposure, crucial in effective therapy (Morrison and Ressler, 2014). We chose to use EDA as our biofeedback measure, as heart-rate based physiological responses have proven not to be as sensitive in VR environments as *in vivo* (Norrholm and Jovanovic, 2018).

CHAPTER 3

EXPERIMENTAL DESIGN

3.1 ETHICAL APPROVAL

The present study received approval from the Health Research Ethics Committee 1 of Stellenbosch University (Ethics ref nr: `N18/10/108`). All participants provided written informed consent.

3.2 STUDY PARTICIPANTS

The present study consists of a control sample collected as part of the parent study looking at the utility of utilizing VR to examine stress in Schizophrenia. Inclusion criteria were healthy adults aged 18 to 45. Exclusion criteria were: a serious or unstable medical condition, educational level $<$ Grade 7, acute substance intoxication or current DSM-V diagnosable condition on screening, apart from Acrophobia (American Psychiatric Association, 2013). Participants were recruited from the Stellenbosch Faculty of Engineering and Faculty of Medicine and Health Sciences post graduate student population as well as friends/family members.

3.3 STRESS RESPONSE MEASURE

3.3.1 EDA biofeedback unit prototype

Recent advances in microcontroller technology allows reasonably accurate measurement of resistance/conductance without the need for specialized equipment in the field (Makan *et al.*, 2019). The current EDA measurement technique is based on work by Makan et al., who utilized an Arduino UNO for the measurement of resistance using a voltage divider and the Arduino 10-bit Analog-to-Digital Converter (Analog-to-Digital Converter (ADC)) (2019) without the

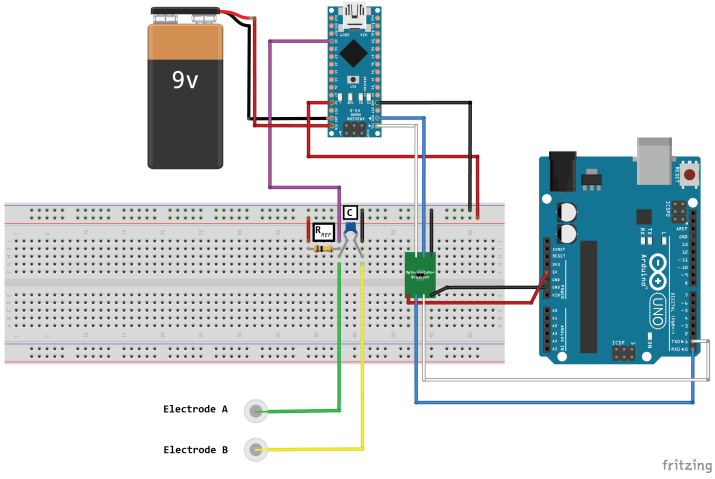


Figure 3.1: Schematic of the EDA monitor

need for additional amplification.

Figure 3.1 (Page 21) shows a schematic of the EDA measuring prototype designed to provide biofeedback in a VR environment. The prototype is constructed around a voltage divider consisting of a reference resistor (R_{REF}) and the skin variable resistance over electrodes A and B (R_X), which were attached to the participant. An Arduino nano (CH340 USB chipset) generic model was used to read the variable voltage. A 10 nF ceramic capacitor was used to reduce dynamic loading effects and noise (Makan *et al.*, 2019). The Adruino is powered by an external 9 volt battery. The Arduino nano delivers a 5 V (V_{REF}) to the voltage divider. To decrease signal noise as well as for saftey reasons, the Arduino nano and voltage divider circuit are electrically isolated by an opto-isolator (Makan *et al.*, 2019). A software serial connection is used in a second Arduino UNO (R3). The Arduino UNO then relays the serial information received from the opto-isolator to the connected PC. For electodes. We use Kendall H59P 8mm cloth electrodes.

Table 3.1 on page 22 shows the parts list showing that the prototype is rela-

tively in-expensive to construct.

Table 3.1: Parts list and total cost of the EDA biofeedback prototype

Part	Price (ZAR)
Sparkfun opto-isolator	R90
Arduino UNO R3 (Generic)	R138
Arduino Nano (CH340 USB Chipset)	R79
1% precision 100 kΩ metal film resistor	R1.37
10 nF ceramic capacitor	R 1
Total	R309

As we apply an external voltage to be able to measure the skin resistance, our current method is *exosomatic*. We use what is referred to by Boucsein *et al.* as the *quasi-voltage* method (2012), as we measured the voltage change over the reference resistor.

To calculate the changes in skin conductance (G), we can express the resistance measured in the voltage divider in terms of the reference resistor R_{REF} and the digital reading of the Arduino ADC (x). Firstly, as V_{REF} and R_{REF} are known, the input voltage can be expressed as:

$$V_{IN} = \frac{R}{R + R_{REF}} V_{REF} \tag{3.1}$$

Given a 10-bit Digital-to-Analog Converter (Digital-to-Analog Converter (DAC)) range of $N = 2^{10}$ values, the input voltage to the ADC (V_{IN}) can be calculated from the ratio of the ADC reading to N multiplied by the reference voltage:

$$V_{IN} = \frac{x}{N} V_{REF} \tag{3.2}$$

The unknown resistance (R) can be given as a function of the ADC reading x:

$$R = \frac{R_{REF.x}}{N - x} \tag{3.3}$$

Given (2.1), we can calculate the conductance (G):

$$G = \frac{N - x}{R_{REF}.x}[\mu\text{S}] \tag{3.4}$$

Following (3.4), C++ Arduino code is loaded onto the Arduino Nano, where conductance measured by each Arduino cycle in terms of the digital input reading at A0 (x_{A0}) (See Figure 3.1):

$$G = \frac{N - x_{A0}}{R_{REF}.x_{A0}}[\mu\text{S}] \tag{3.5}$$

3.3.2 Relative error estimation and optimization

The optimal accuracy of the present system, is largely driven by the precision of the reference resistor (R_{REF}) and the in-built error of the Arduino ADC. Makan *et al.* shows that the accuracy is non-linear, dropping off at very high as well as very low measured resistances (2019). Given the range of skin conductance is normally between 5 and 25 μS, an optimal measurement error can be obtained by selecting an optimal reference resistor. Working in reverse from (2.2), we can express resistance as the reciprocal of conductance:

$$R[\text{k}\Omega] = \frac{1,000}{G[\mu\text{S}]} \tag{3.6}$$

A range of 5 to 25 μS is therefore equivalent to a measured resistance range from 40 to 200 kΩ.

Makan *et al.* shows that the optimal resistance value can be expressed as:

$$R_{REF} = \sqrt{R_{max} \cdot R_{min}} \tag{3.7}$$

Hence:

$$R_{REF} = \sqrt{40\,\text{k}\Omega \cdot 200\,\text{k}\Omega} = 89.44\,\text{k}\Omega \tag{3.8}$$

Following Makan *et al.*, the measurement error can be calculated as follows:

$$\left|\frac{\Delta R}{R}\right| \approx \left|\frac{\Delta R_x}{R}\right| + \left|\frac{\Delta R_r}{R}\right| \approx \left|\frac{N}{x \cdot (N-x)}\Delta x\right| + \left|\frac{\Delta R_{REF}}{R_{REF}}\right| \tag{3.9}$$

By entering the value of our reference resistor from (3.8), we come to an acceptable measurement error of 1.9 %. Using a 100 kΩ reference resistor, we reach a similar accuracy of 2 %. We can further calculate the range for the optimal resistance values as follows for the new 100 kΩ reference resistor ((Makan *et al.*, 2019)):

$$x_{max,min} = \frac{N}{2} \pm \sqrt[2]{\left(\frac{N}{2}\right)^2 - \frac{N \cdot \Delta x}{\left|\frac{\Delta R}{R}\right| - \left|\frac{\Delta R_{REF}}{R_{REF}}\right|}} \tag{3.10}$$

Using equation 3.3, we can calculate the resistance range:

$$R_{max,min} = \frac{\frac{R_{REF}}{N}}{\frac{N}{x_{max,min}} - 1} \tag{3.11}$$

Using equations (3.10) and (3.3), we can calculate that given a reference resistor falling between 36 and 275 kΩ, which following (2.2) results in an optimal measurement between 3.6 to 27.8 μS. As the 10-bit Arduino can measure a maximum of 1024 ($N = 2^{10}$) increments, this results in $27.8 - 3.6/1024 = 0.02\,\mu$S increments. This is still within range of the minimum 0.05 μS threshold for a SCR to occur, showing that the present setup is suitable for the detection of standard SCRs.

3.4 CLINICAL ASSESSMENTS

All participants were briefly assessed clinically by a general practitioner for current medical, psychiatric or substance abuse disorder. Note that not all of the data on the CRF was captured in healthy controls. Participants completed a modified computer familiarity questionnaire based on that developed by

Jamieson et al. 1998, as well as the iGroup presence questionnaire (IPQ), to measure the felt realism of the VR environment (Brewster *et al.*, 2019). Visual heights intolerance as well as acrophobia were assessed by the Visual Height Intolerance Severity Scale (Visual Height Intolerance Severity Scale (vHISS)) (Huppert *et al.*, 2017).

Acrophobia was diagnosed according to the vHISS, using the given DSM-V criteria (American Psychiatric Association, 2013):

- At least one of the vegetative symptoms (i.e. trembling, palpitations, inner agitation, and sweating/moist hands) from List A (See Table 3.2, page 25).
- Two other additional symptoms from List A (See Table 3.2, page 25).
- A positive response to item 6 (i.e. duration of at least 6 months) of the severity scale (yes)
- A positive response to items 9 (i.e. Do you feel very intense fear or extremely strong fear when exposed to heights?) and 10 (i.e. I try in advance to avoid exposure to heights)

Table 3.2: vHISS Bodily symptoms when exposed to heights (Huppert *et al.*, 2017). Reproduced under CC license.

Bodily symptom
Trembling
Palpitations
Inner agitation
Sweating/moist hands
Light-headedness
Postural ($to - and - fro$) dizziness
Weakness in the knees
Instability of stance and gait
Malaise/queasy feeling in the stomach
Oppression
Fearfulness
Mental image of falling
Gait disorder
Others

Additionally the participants were asked at the end of the study to rate their experience using the biofeedback system, using the following questions:

- Rate your experience using the biofeedback (Poor/OK/Good/Excellent)
- How closely did the feedback resemble your anxiety experience? (Lower/As/Higher than expected)
- Which do you think was more accurate in terms of the anxiety/stress you experienced? (My own/both/the biofeedback)

3.5 RENDERING HARDWARE

3.5.1 PC hardware

The environment was rendered on a Intel(R) Core(TM) i5-8300H CPU @2.30GHz Lenovo laptop (Model Y740-15ICHg), with 16 GB of RAM, running 64 bit Windows 10. We used a dedicated NVIDIA GeForce RTX 2060 graphics card.

3.5.2 Head Mounted Display

An Oculus Quest 2 headset was used, connected via USB-C 3.1 using a Oculus Link cable, with two standard motion controllers to interact with the environment.

3.6 UNREAL ENVIRONMENT SETUP

3.6.1 Basic Setup

The present project was implemented in Unreal version 4.24.2 (`www.unrealengine.com`) using their built in blueprint scripting environment as well as C++ implementations where appropriate. A standard Virtual Reality content template was used as the base to implement the Oculus Quest 2 motion controllers as well as the head mounted display. A standard sky sphere as well as simple directional lighting was used. The built in frame-rate tool was used periodically to

maintain a target frame rate of 60 $Hz+$ to avoid nausea and dizziness ((Yao *et al.*, 2014)).

3.6.2 Environment

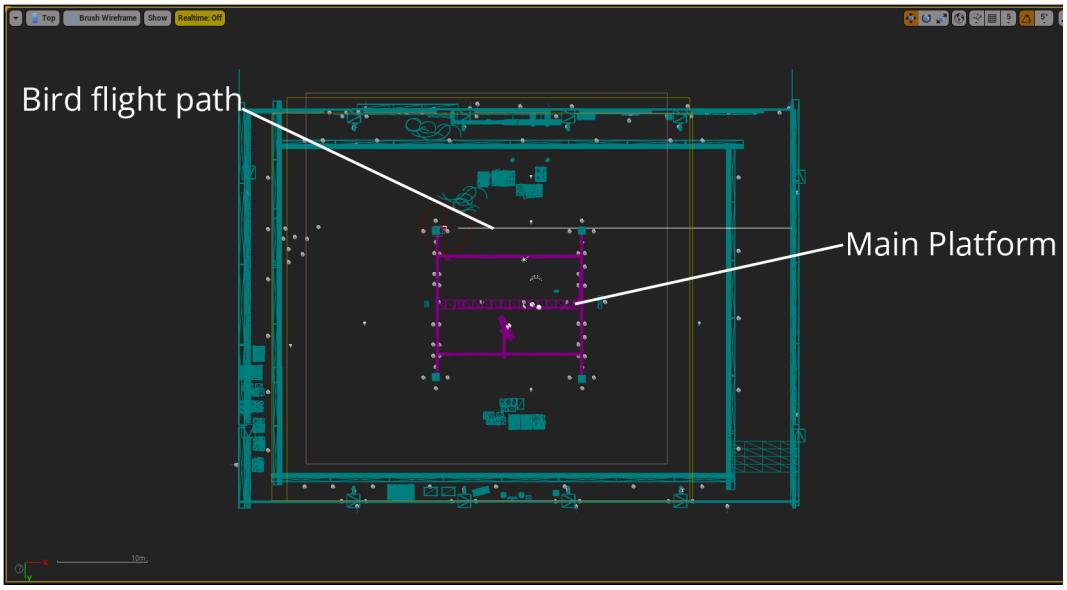


Figure 3.2: General Environment

The environment was assembled from several free to use content packs, as well as commercially licensed content. The environment resembled a warehouse environment measuring 62x45x28 meters (See Figure 3.2, page 27). Three dimensional sound settings were used, to create a subtle echo in environment sounds, to further emphasize the size of the environment. A central suspended platform (i.e. the main platform) was created roughly in the center of the environment (See Figure 3.7, page 31). Platform sounds would be timed with the platform movements. The character controller was placed at one end of the main platform, allowing participants to look upwards comfortably to get an optimal vantage point of the environment. The character controller (i.e. where the participant would appear) was placed at the edge of the platform to further enhance the sense of height via perspective (See Figure 3.4, page 29). This also served to create a believable support mechanism for the platform (See Figure 3.4). An additional intermediate platform was placed 8.7 meters above

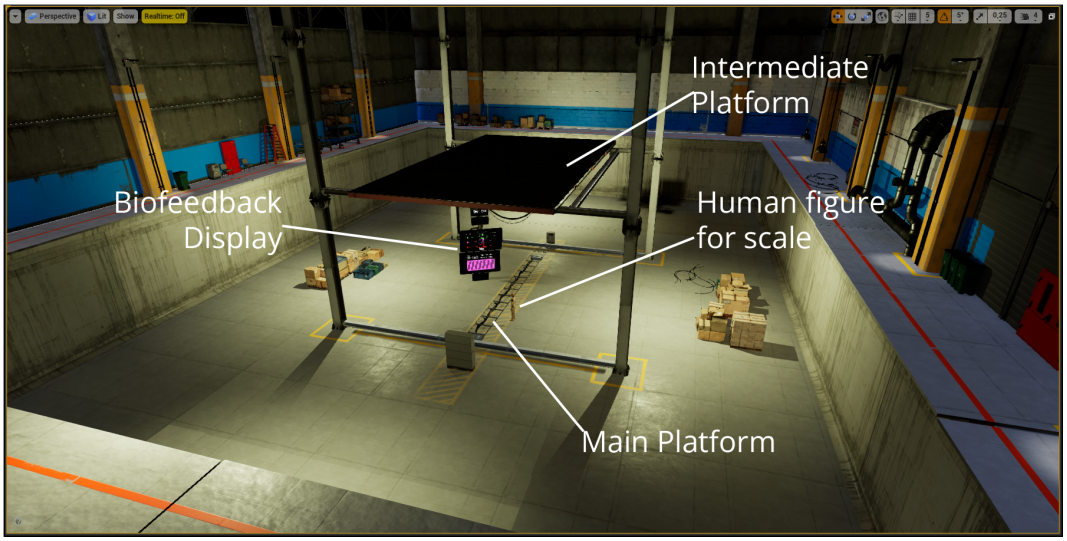


Figure 3.3: Elevated platform perspective view

the participant's head (See Figure 3.7, page 31). This would avoid premature anticipatory arousal while the baseline data was collected by obscuring the view of the full height of the warehouse.

3.6.3 Biofeedback

To the immediate left of the participant, suspended in a believable way from the scaffolding, participants were presented with a biofeedback screen array (See Figure 3.5). To avoid the task length becoming frustrating or distracting, the time since the start of the task was presented on the clock screen. Participants were told the task will take around 17 minutes to complete. The screen immediately below the clock (i.e. the max feedback screen) displays, "New High" whenever the participants EDA reached a new maximum level. This was done to keep the participants' attention on the biofeedback screen array. Below this screen was the participant feedback screen, where participants gave their own subjective feedback on their current arousal state and the tolerability of the environment. Below the EDA feedback screen, participants were given the current EDA reading, with bar graphs showing the immediate preceding 20 readings, as well as the minimum and maximum readings. Par-

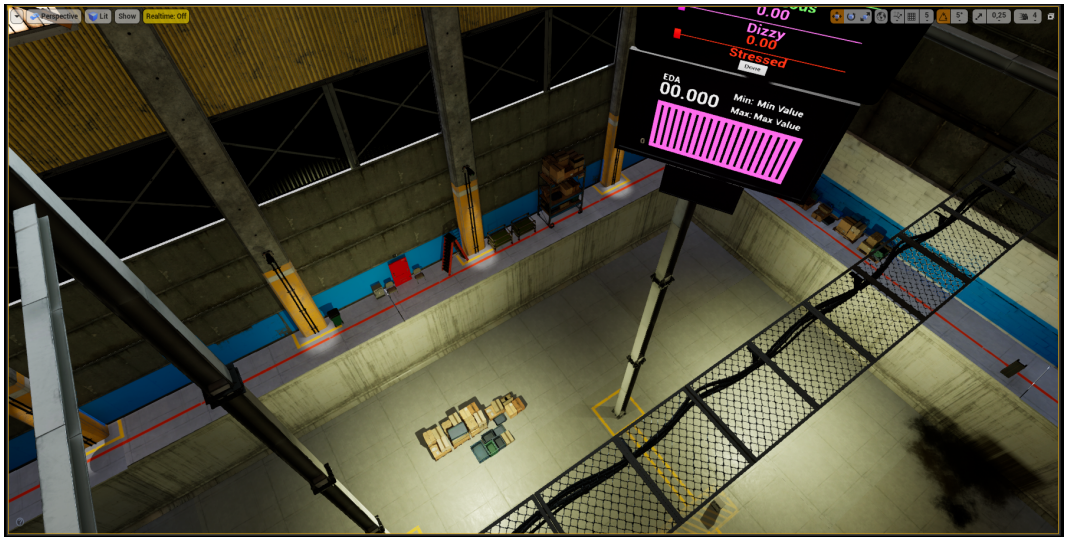


Figure 3.4: View from the platform at full height

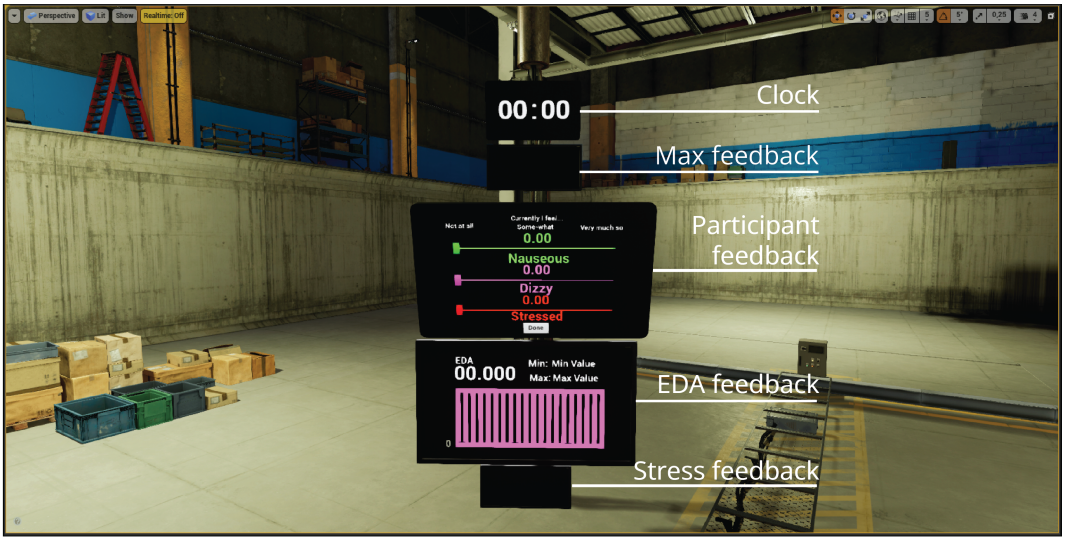


Figure 3.5: Biofeedback screen array

ticipants were informed that for the first five minutes their average baseline measurement would be collected. Afterwards, the mean EDA level would be displayed as a blue line perpendicular to the bar display on the EDA feedback screen. It was explained to them that any reading that exceeds the mean reading collected at baseline, would trigger a "Stressed" display on the lower stress feedback screen. The stress feedback screen will otherwise read "Relaxed". This display continued until the end of the VR scene.

3.6.4 Task design

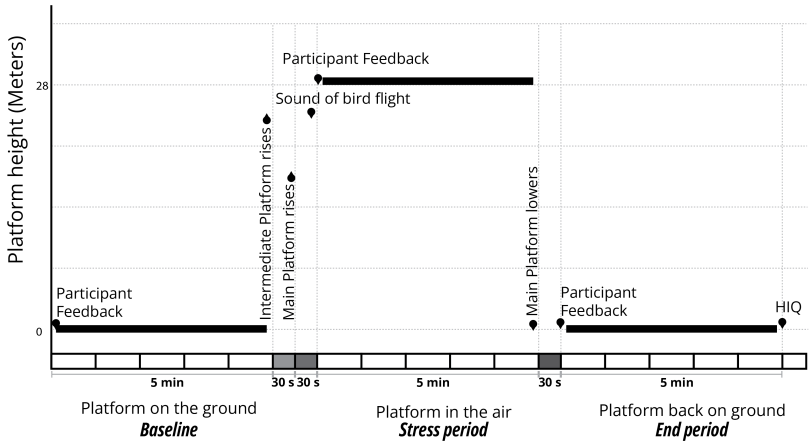


Figure 3.6: Task design overview.

The task was presented in 5 minute intervals, with the platform taking an additional 30 seconds to rise/lower to and from the target height (See Figure 3.6, page 30). The first 5 minutes served as a baseline measurement, with the intermediate platform (See Figure 3.7, page 31) in place. Participants would be prompted to record their current levels of nausea, dizziness and how stressed they felt on a 1 to 5 point Likert scale using the motion controllers. After 5 minutes the intermediate platform would rise to the top of the warehouse, revealing the full height of the environment (See Figure 3.8, page 32). The

main platform started to rise at this point. The feedback screen proceeded to count up the current platform height. The platform took around 30 seconds to reach the full height of the environment (i.e. 28 meters). To additionally emphasize the full height of the platform, an animated bird would be startled into flight. Shortly after the platform reached maximum height, the participant was prompted to report on their nausea, dizziness and stress levels as before. The platform remains in place for 5 minutes, after which it lowered to the baseline level once more. Once the platform reached the floor, participants repeated the assessment. They would then wait a further 5 minutes. Before the VR scene was ended, the participant filled in the HIQ (Steinman and Teachman, 2011) inside of the environment on the feedback screen. The full length of the VR task was around 17 minutes for each participant.

Figure 3.7: The intermediate platform

3.6.5 Unreal implementation

Similar to the environment, the biofeedback was implemented in the Unreal Engine 4.24.2 as part of the same project. For an overview of the C++ and Blueprint implementation see Figure 3.9 on page 33. The blue flowchart figures are code sections implemented in Unreal's visual scripting language blueprint. Red sections are code portions using the **UE4Duino Unreal plugin**. Black

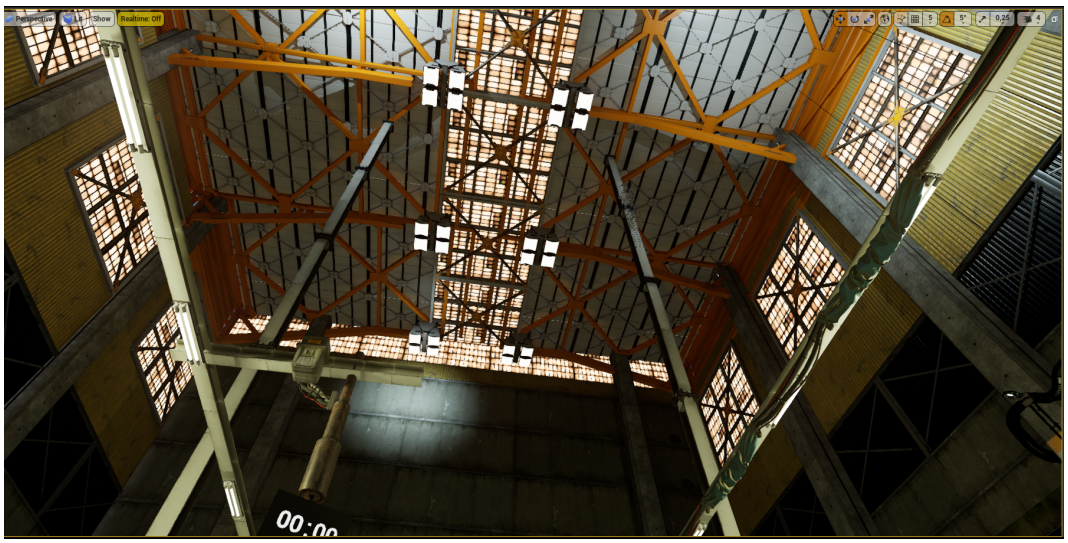


Figure 3.8: View of the full height of the environment after the intermediate platform is raised

sections are custom C++ implementations created for file handling as well as outlier management. White portions are software events.

On startup of the environment, UE4Duino is used to open an available serial communications (COM) port. The twenty feedback bars are also initialized using 2D meshes. A 20 element float-array is also initialized (EDA data array). As above, participant feedback is collected via the participant feedback screen (See Figure 3.5, page 29). Unreal is designed to execute selected code portions in sync with the screen refresh rate. In our implementation, this occurred just below our target 60 Hz. On every screen refresh data is read from the COM port. This data is then stored in the EDA data array. This data is then scaled to the max reading collected for later display. A timestamp is also stored in a separate array, which is used in our **Ledalab** analysis (See Data Analysis). Custom C++ code was used to define the interquartile range, i.e. data between the first and third quartiles. Data points falling outside this range were identified as outliers and removed. The mean of the EDA data array was then calculated and displayed on the biofeedback screen (See Figure 3.5, page 29). The display bars were then scaled according to the EDA data

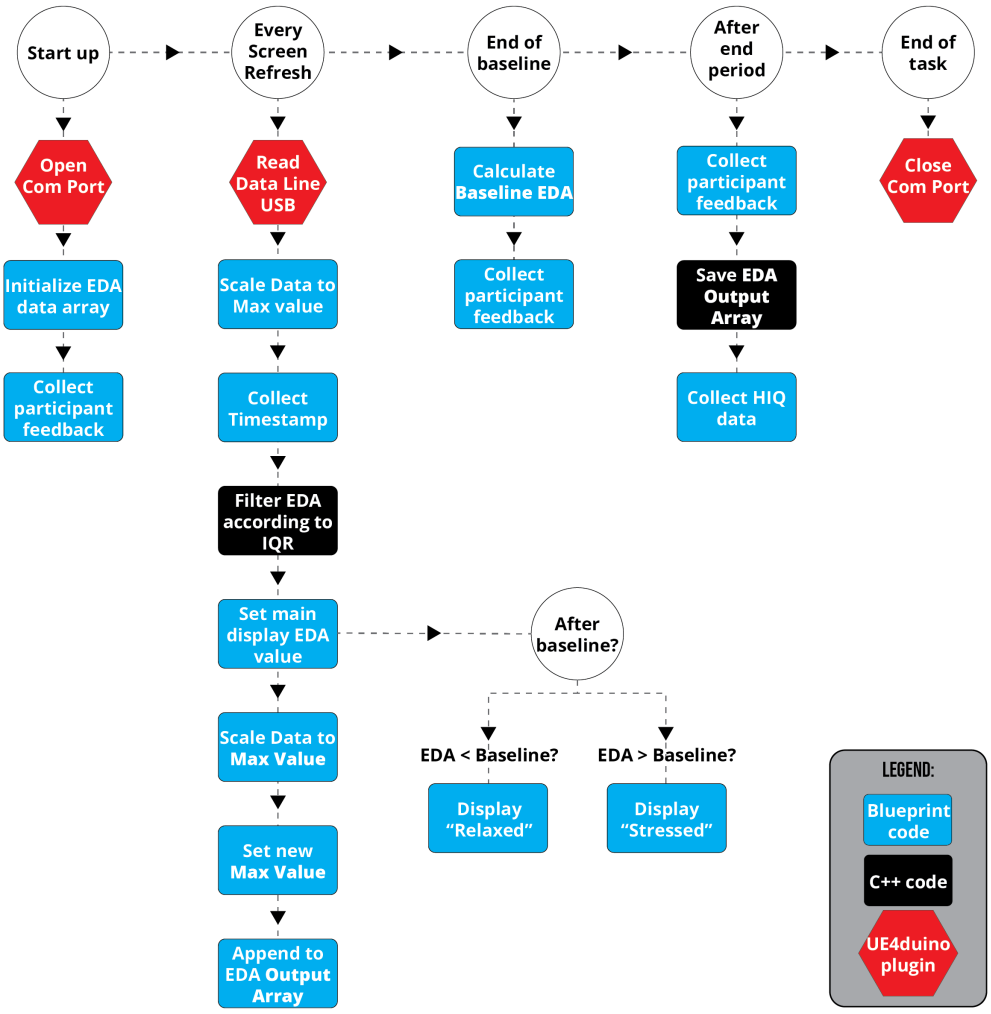


Figure 3.9: Unreal implementation overview.

array, after the data was scaled according to the max value. The EDA data array as well as the timestamp, was then appended to the EDA output array.

As mentioned in the task design section, the mean of the EDA output array was calculated after 5 minutes (i.e. at the end of the baseline period) and displayed on the biofeedback screen. After this point, should the displayed EDA value on the biofeedback screen exceed the baseline, "Stressed" would be displayed on the bottom screen (See Biofeedback section above for more detail). After the end period (See Figure 3.6, page 30) the EDA output array was saved using a custom C++ script. At the end of the task, after the Heights Interpretation Questionnaire (Heights Interpretation Questionnaire (HIQ)) data was collected (Steinman and Teachman, 2011), the COM port is closed using the UE4Duino plugin.

3.7 DATA ANALYSIS

3.7.1 Demographics

Participant data was entered and retrieved from an online **Red Cap database** by the study clinician.

3.7.2 Data preprocessing

Custom analysis scripts were implemented in MATLAB 2019a to import the Red Cap database, the participant feedback, as well as the raw EDA data collected during VR exposure. The data was preprocessed by applying a high-pass filter (0.05 Hz) as well as a moving filter window set to 100 ms. The EDA data was averaged for the Baseline, Stressed as well as the End Period. Note that the main platform rise and lowering (See Figure 3.6 on page 30) as well as the raising of the intermediate platform was included in the stress period for the analysis. These data was then combined and exported for analysis in **IBM SPSS statistics Version 27**.

3.7.3 VR side effects

Side effects reported in VR (i.e. dizziness, nausea) were entered in a repeated measures analysis of variance (RM-ANOVA), with baseline, stress period as well as end period as time points. Departure from sphericity was examined using Mauchly's test of sphericity. Any departures were adjusted for using the Greenhouse–Geisser correction. In the presence of a significant within-subjects main effect, *Post hoc* tests were conducted to examine for specific differences between the time-points. These tests were corrected for using Fishers Least Significant Difference (LSD) correction for multiple comparisons. Finally EDA measures were correlated using Pearson's correlations, with the mean EDA as well as CDA measures to test for a confounding influence of the side-effects on physiological responses.

3.7.4 Subjective stress responses

Similarly, subjective stress responses were also entered into a RM-ANOVA, correcting for deviations from sphericity. *Post hoc* tests were also carried out in a similar fashion. To examine whether the results were mostly the result of responses by participants with acrophobia, acrophobia participants were removed and the data re-analyzed.

3.7.5 Mean EDA responses over time

Prepocessed EDA data was first visually inspected to determine when the biofeedback would have indicated a "Stressed" vs "Relaxed" state. As for the subjective stress responses, mean EDA responses were entered into a RM-ANOVA analysis. The change in subjective stress measures between the baseline and stressed period was then correlated with the same change in mean EDA response using a Pearsons correlation. This was done to confirm if the EDA responses seen was a reflection of the subjective stress experienced due to the rising platform. As with the previous analysis, acrophobia participants

were removed from the analysis, and re-analyzed to verify the robustness of the findings.

3.7.6 Clinical correlates

To further cross validate the given biofeedback responses, an exploratory correlation analysis, using Pearson's correlations was conducted, comparing the sub-categories of the HIQ collected in VR with the mean EDA response during the stressed period. As this was a confirmatory as well as exploratory analysis, no multiple comparisons correction was used.

3.7.7 CDA analysis

As the mean EDA signal can be contaminated by overlapping phasic skin conductance responses, we conducted a CDA analysis in **Ledalab** using the preprocessed EDA data. The number of CDA events were entered as above into a RM-ANOVA for the baseline, stressed and end-period. *Post hoc* tests were conducted in a similar fashion. Acrophobia participants were added and then removed as before.

3.7.8 Participant feedback

Participant feedback scores were qualitatively examined, to determine their general experience of using biofeedback, how accurate they perceived the biofeedback to be and if they tended to trust their own experience or the biofeedback instead.

CHAPTER 4

RESULTS

4.1 DEMOGRAPHICS

22 participants were recruited over a period of 2 months (See Table 4.1). All received tertiary education. All participants were seen by the study clinician. No participant gave a history of any psychiatric or physical illness that would confound the study findings. This includes severe co-morbid depression, substance abuse or other severe anxiety disorders that could lead to heightened stress sensitivity on their own. All participants were highly familiar with computers. We found no relationship between computer familiarity and EDA values. This could potentially be a ceiling effect, as all participants scored close to the maximum of 100 (See Table 4.1).

Four of the participants had acrophobia on the vHISS scale. The distribution of the vHISS scores was non-normal on examination, revealing two distinct peaks with a relatively high standard deviation (SD= 7.21) When we removed the participants with acrophobia, the distribution took on a more normal shape with less inter-subject variability (SD= 3.26). We therefore considered a leave out analysis after each main analysis to confirm that our results were not driven by extreme arousal by those with acrophobia.

Similarly, presence scores had a relatively wide standard deviation (SD=5.35). The presence scores were, however, normally distributed with no outliers. The mean value of 7 was comparable to those reported in the literature (Brewster *et al.*, 2019). However, we found no relationship between presence scores and EDA values in our present study.

Table 4.1: Participant demographics

	Mean	SD
Sex (M/F)	6/10	
Mean age (years)	28.64	5.37
Presence Score	7.14	5.35
vHISS total score	8.52	7.21
Computer Familiarity Score	96.33	4.80

4.2 VIRTUAL REALITY SIDE EFFECTS

No severe nausea was reported by any of the participants, nor any excessive dizziness. Subject self-reported nausea level reported while immersed in the VR environment remained stable throughout the task, with no significant deviation from the baseline level ($F(2, 15) = .469, .635$). There was a small, but significant main effect over time, showing an increase in subjective dizziness self-reports ($F(2) = 5.164, p = .010$). LSD corrected *post hoc* tests showed a significant increase in dizziness in both the stress period ($p = .003$) and the end period ($p = .041$). All scores were below 3 on the 1 to 5 Likert scale. Similarly, a correlation analysis showed participant dizziness and nausea were not related to SC levels in this sample.

4.3 SUBJECTIVE STRESS RESPONSES

All subjects showed a significant main effect for change in height for self-reported stress level ($F(1.490) = 5.174, p = .020$), showing that they experienced increased subjective levels of stress as the platform rose (See Figure 4.1). LSD corrected *post hoc* tests revealed that there was a significant increase for both the stress period ($M_{STRESS} = 1.765, p = .006$) as well as the end period ($M_{END} = 1.53$) relative to the baseline ($M_{BASELINE} = 1.059, p = .030$). The results remained significant when the participants with acrophobia were removed.

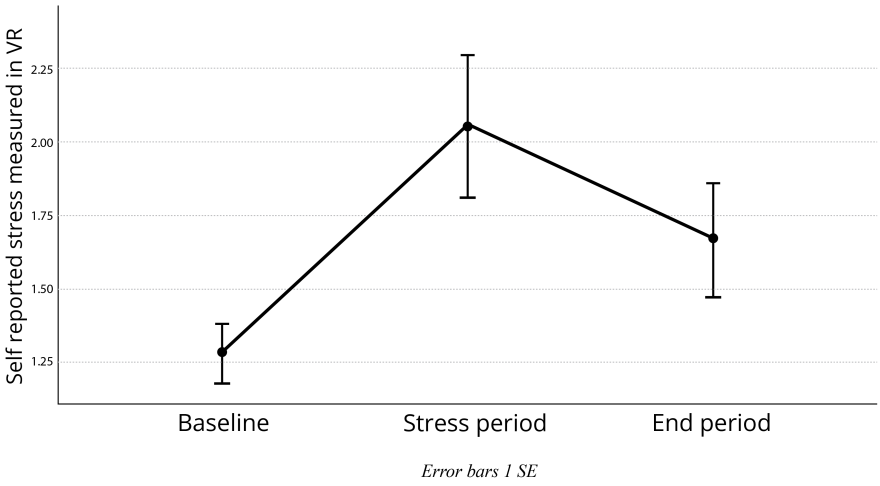


Figure 4.1: Subjective stress over time.

4.4 MEAN EDA RESPONSES OVER TIME

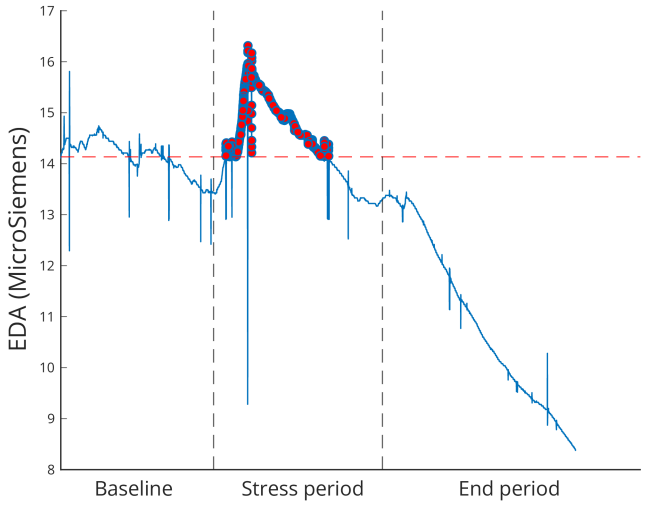
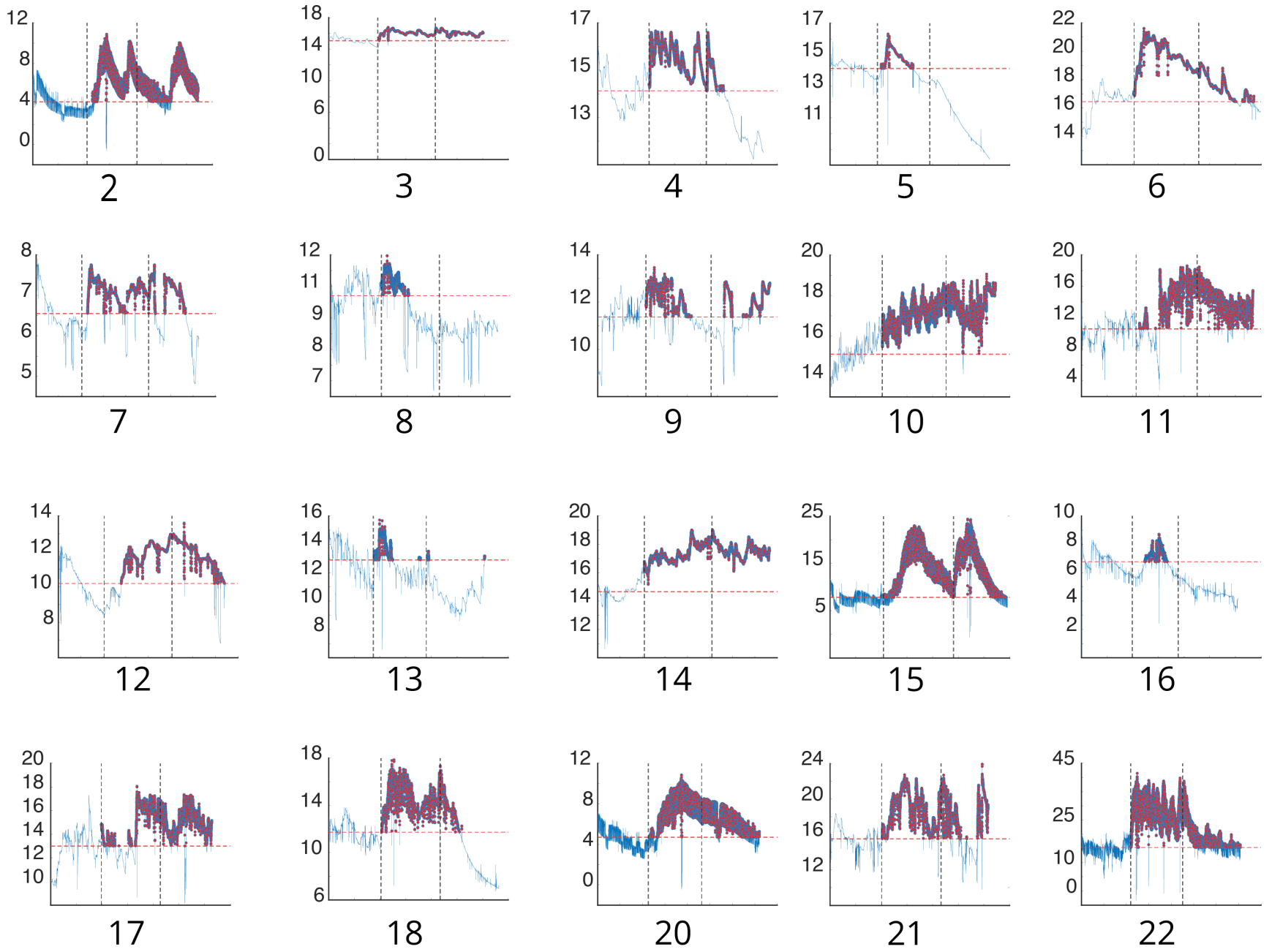


Figure 4.2: Subject showing an ideal response.

As expected, participants showed a normal raw skin conductance level, ranging between 4 to 16 μS at baseline. This is comparable to the range given in the literature of between 1 μS and 20 μS (Gersak, 2020). Figure 4.2 shows an ideal response: a low stable baseline, with mean raw SC exceeding the

baseline during the stressor and a decrease as the platform was lowered to the ground. When all the subjects' raw signal data was examined in this way (See Figure 4.3), it showed 4 out of the 20 subjects had ideal responses. Two more subjects briefly had elevated raw SC values which returned to baseline in the 5 minute period. The remaining subjects all had elevated SC responses for the remainder of the task. However, all subjects had increased levels of SC after the start of the stressor.



Mean raw SC level showed a significant main effect for change in platform height ($F(2) = 7.635, p = .002$), with LSD corrected *post hoc* tests showing a significant rise for mean SC level (p=.004) for the stress period but not for the end period (p=.109) relative to the baseline (See Figure 4.4). This demonstrates that subjects had an elevated SC relative to baseline only during the stress period. When the four participants with acrophobia were removed from the analysis, the results remained significant.

4.5 CLINICAL CORRELATES

As it is still unclear whether these changes, which were presented to the participants as live biofeedback, reflect general arousal, or specific stress related to heights, further exploratory tests were conducted. Indeed, the relative increase in subjective stress was significantly related to the increase in mean SC level during the same period (r=.673,p=.002). This shows increased SC levels are related to increased anxiety experienced relative to the height increase. Furthermore, the The Heights Interpretation Questionnaire items "I did not feel safe [on the platform]" and "I feel like I might hurt myself [on the platform]" items also significantly predicted mean SC measure during the stress period (r=.479,p=.038;r=.564,p=.012).

4.6 CDA ANALYSIS

The CDA levels supported the biofeedback data presented to the participants, showing a significant main effect for change in platform height ($F(2) = 25.290, p < .001$). LSD corrected *post hoc* tests showed that CDA deviated significantly from the baseline during the stress period ($p < .001$) as well as during the end period (p=.031) (See Figure 4.5. It should be noted that subjects had significantly less CDA responses at the end period than during the baseline. As with the other measures, the results remained significant when the participants with acrophobia were removed.

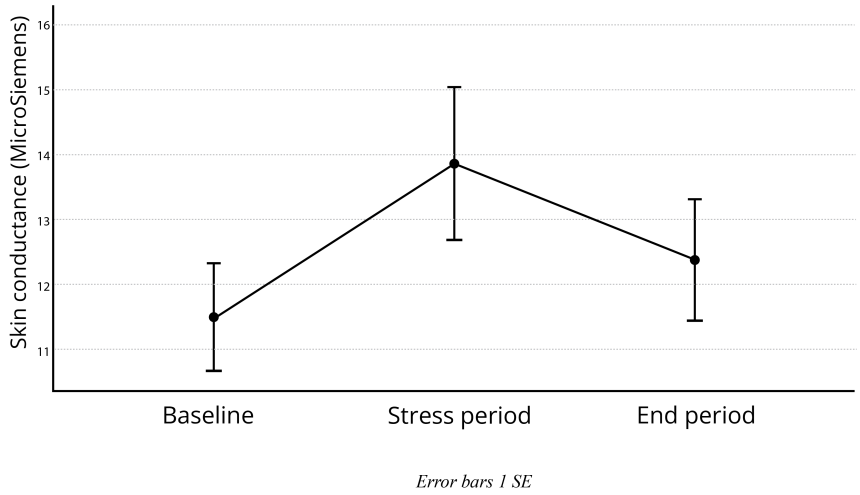


Figure 4.4: Mean skin conductance over time

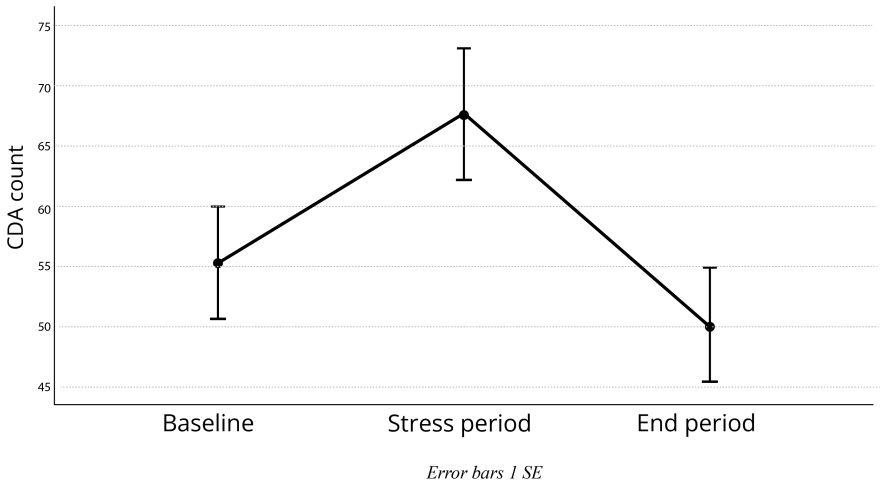


Figure 4.5: Mean CDA counts over time

4.7 PARTICIPANT FEEDBACK

In general, all participants had a positive experience, with 2 of the 21 participants rating their experience using the biofeedback as "OK", with the rest of the participants rating it as "Good" (See A, Figure 4.6). The majority of the participants (n=13) felt like the biofeedback gave a good reflection of their own anxiety experience on the platform. A large portion of the participants, however, felt that the readings were higher than expected (n=7), with only one participant rating it as lower than expected (See B, Figure 4.6). Interestingly, the majority of the participants felt that both the biofeedback and their own feelings accurately reflected their experience, with five participants still trusting their own feelings more. A few trusted the biofeedback more than their own experience (n=3) (See C, Figure 4.6).

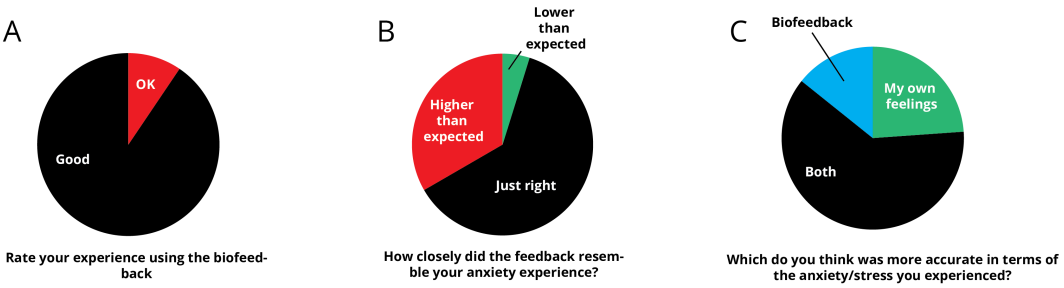


Figure 4.6: Subjective rating of the biofeedback experience.

CHAPTER 5

DISCUSSION

Here we developed and tested a cost effective VR acrophobia environment with biofeedback in a sample of 22 participants, 4 of whom had clinically measurable acrophobia. Participants were otherwise healthy. To our knowledge biofeedback using EDA has not been evaluated in a VR environment in the context of height exposure. Our results show an expected significant rise and fall of the SC responses, corresponding with the ascent and descent of the platform. Change in SC responses correlated significantly with changes in self-reported anxiety, and not with common VR related side effects. Furthermore, SC measures did correlate with clinical visual heights intolerance measures. Offline phasic CDA analysis confirmed the biofeedback measures presented to the participants. All participants, including those with acrophobia, reported a positive experience with the biofeedback. The majority of participants felt that the biofeedback measures corresponded with their own anxiety experiences. Most reported trusting both their own experience as well as that of the biofeedback measure. Our findings suggest that the use of VR based biofeedback as a cost-effective treatment adjunct in people with acrophobia warrants further investigation.

In our current environment we measure little to no nausea nor dizziness experienced by our participants. These side-effects did not have a significant impact on our SC measures and in turn the biofeedback presented to the participants. Simulator sickness is quite common in VR environments, ranging from 22 to 80 % of participants (Kim *et al.*, 2021). We speculate that our relatively low level of simulator sickness is firstly a result of our use of an updated HMD, as our own in-house simulator sickness levels dropped from 19 % study attrition using the Oculus Devkit 2 (Vanbeylen, 2016) to zero for the present study. However, it is difficult to compare the headsets directly, as the full specifications of our current HMD has not yet been released. Secondly, our environment is

stationary. Although subjects can move around in the environment, they were not required to do so. Subject movement inside a VR environment is usually associated with increased levels of simulator sickness (Kim *et al.*, 2021). Given our small sample, we cannot rule out the impact of simulator sickness on our biofeedback in a larger sample. Larger samples using our environment will need to be collected.

We measured a strong and predictable SC response associated with the change in height of our VR platform. Similar to previous studies, small increases in subjective stress levels were accompanied by relatively strong increases in tonic SC levels (Diemer *et al.*, 2016). An increase in self-reported stress levels are reported in some studies (Meehan *et al.et al.*,2002, Simeonov *et al.et al.*,2005, Wilhelm *et al.et al.*,2005, Cleworth *et al.et al.*,2012) but not in others (Diemer *et al.*, 2016). Here we present an environment that is able to induce physiological responses with corresponding increases in self reported stress levels. Not only is this important in terms of task validity, but also makes it possible to detect paradoxical responses in participants, i.e. increased stress responses do not always result in a positive increase in SC (Taylor *et al.*, 2021). Most studies report a need for participants to look down before a physiological response could be elicited (Diemer *et al.*, 2016). We speculate our environment induces a fear of heights regardless of vantage point, as the height is appreciable from several angles which includes having a roof, increased perspective to the rails attached to the platform as well as other implicit cues such as an increased reverb in the environment with birdsong that suggests a large, elevated environment. Previously tested acrophobia environments include a small pit room (Meehan *et al.*, 2002), skyscraper environment (Diemer *et al.*, 2016) or having participants gaze over an indoor safety railing (Simeonov *et al.*, 2005). Importantly none of these environments gave a gradual increase in heights. Diemer et al. 2016 teleported participants from one scene to another. However, control was given to the participants to walk towards the edge. Of note,

simulated objective danger such as in our present design (i.e. the lack of physical railings) was only present in one of these studies (Diemer *et al.*, 2016). Moreover, no additional props were needed in our present design such as a real world plank (Diemer *et al.*, 2016). The present VR environment is therefore arguably more practical for use in clinically settings. The examination of specific acrophobia related cues that cause a relative increase in anxiety levels, fall outside of the scope of the present work, however. Furthermore, our present study is limited by not having gaze tracking. The particular visual stress cues are therefore difficult to determine. Interestingly, the majority of studies that examine physiological responses in VR, report on tonic but not phasic responses (Meehan *et al.*,2002, Simeonov *et al.*,2005, Wilhelm *et al.*,2005, Cleworth *et al.*,2012). Indeed, we found that phasic responses in our environment correlated significantly with participant-reported anxiety, which validates the biofeedback received by participants.

We found several clinical correlates with increased anxiety responses. This includes participants reporting that the environment objectively did not feel safe and they were scared that they were going to injure themselves, as reflected on the Heights Interpretation Questionnaire ((Steinman and Teachman, 2011)). This provides further validation that the biofeedback measure was providing a valid feedback to the participants of their current arousal state.

Indeed we found that the majority of participants believed the biofeedback measure to be accurate when compared to their own assessment of their fear response. Previous biofeedback studies also report positive outcomes with biofeedback in stress management (Teufel *et al.*, 2013), although few consider to what extent the participants trust this feedback. Indeed we did find a substantial percentage of participants that rather believe their own assessment over that of the biofeedback. This could potentially have a negative impact on biofeedback as a treatment tool in these participants. It is also possible that participants also under reported their anxiety experiences. Further study into

patient self-assessment is needed.

All participants reported a positive experience in our present environment. Although the option was given to stop the platform should the exposure be excessive, no participant chose this option. Although all our present acrophobia sufferers did indeed reached the maximum height of the platform, our sample is far too small to rule out if our maximum exposure would not prove to be too excessive for participants in the acrophobia population. Treatment trials using the present design is therefore needed.

Given that participants gave positive feedback using the present paradigm and that the physiological analysis corresponded with participant experiences, the present use of biofeedback in VR is valid and should be considered in treatment trials moving forward. Nevertheless, there are a few limitations that should be considered.

Our present design, although safe, is not fully standardized. We use a larger voltage than usual (i.e. 2 volts rather van 0.5 to 1 V) as well as increased current (55 μA vs 10 μA) (Boucsein, 2012). Theoretically the higher voltage allows for a simpler circuit to be constructed and is therefore difficult to compare to previous findings. Although we do indeed detect both tonic and phasic signals using the present prototype model, it should be compared to other designs such as those of Lykken and Venables, (1971), who utilize a lower current with the use of operational amplifiers. The advantages of this would be greater standardization. The lower voltage could also theoretically result in less direct external electrical contamination of the current with the function of the sweat glands (Lykken and Venables, 1971). At present we utilized gel electrodes and not more specialized foam electrodes, because of better adhesion to subjects fingers. As the gel electrode's composition is uncertain at this time, we cannot rule out an effect on hydration state over time. This could theoretically cause signal drift via dermal swelling or relative dehydration over time ((Dormire and Carpenter, 2002)). Although our present task design was set up so that

neither an increasing not a decreasing signal trend would affect our results, in future more standard electrodes should be used.

As mentioned previously, we did not include gaze tracking in our present design. Current HMDs which include gaze tracking are not fully supported by the Unreal platform and are significantly more expensive than our present commercially available headsets. Future work could include gaze tracking to further refine the environment, by investigating which environmental cues are associated with the strongest physiological as well as subjective stress responses.

Advantages of the current biofeedback prototype is that it is cost effective, costing at approximately 309 ZAR to construct (See again 3.1 on page 22). Parts are readily available and supported by software platforms such as the Unreal engine. It is also reasonably sensitive, as it can detect CDA responses in participants with relatively low levels of self reported stress as shown in our study results. Nevertheless, a larger study comparing the present design with a standardized approach will be needed to establish its effectiveness. Additional improvements could be the addition of a small monitor so that the feedback can be used *in vivo* as well as enabling clinicians to monitor the physiological levels of their patients more clearly. Although EDA monitoring can be performed in a cost effective way, Virtual Reality headset costs could still prove prohibitively expensive in resourced constrained regions. Nevertheless, as the technology matures, there doubtlessly will be a drop in price for entry level devices as required in our current implementation.

CHAPTER 6

CONCLUSION

Altough our present prototype biofeedback monitor for use in VR does present room for improvement, it does succeed in our primary aims. Firstly, subjects reported a comparable level of immersion to other studies. This immersion resulted in a significant increase in EDA responses, validating that the present task can indeed increase physiological arousal, as well as a significant increase in subjective stress in a control population. Secondly, we demonstrate its inclusion does not result in any performance dips significant enough to cause VR related side effects. Any minor side effects experienced during the task did not significantly impact on our EDA measures and therefore the biofeedback. Thirdly, the environment can be run on a standard laptop. The EDA monitor is also relatively inexpensive to construct. Given the price of the hardware, future suggested improvements are unlikely to cause a significant increase in price, which should make this therapy accessible to most psychologists. Furthermore, all participants had a good experience with the biofeedback display. The majority indicated that the display was believable. Finally, our EDA results as well as subjective feedback data cross validated each-other, indicating that the biofeedback display was reasonably accurate. The present work indicates that biofeedback in VRET is a promising treatment adjunct.

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