Subjective and physiological reactivity to flight in people with fear of flying

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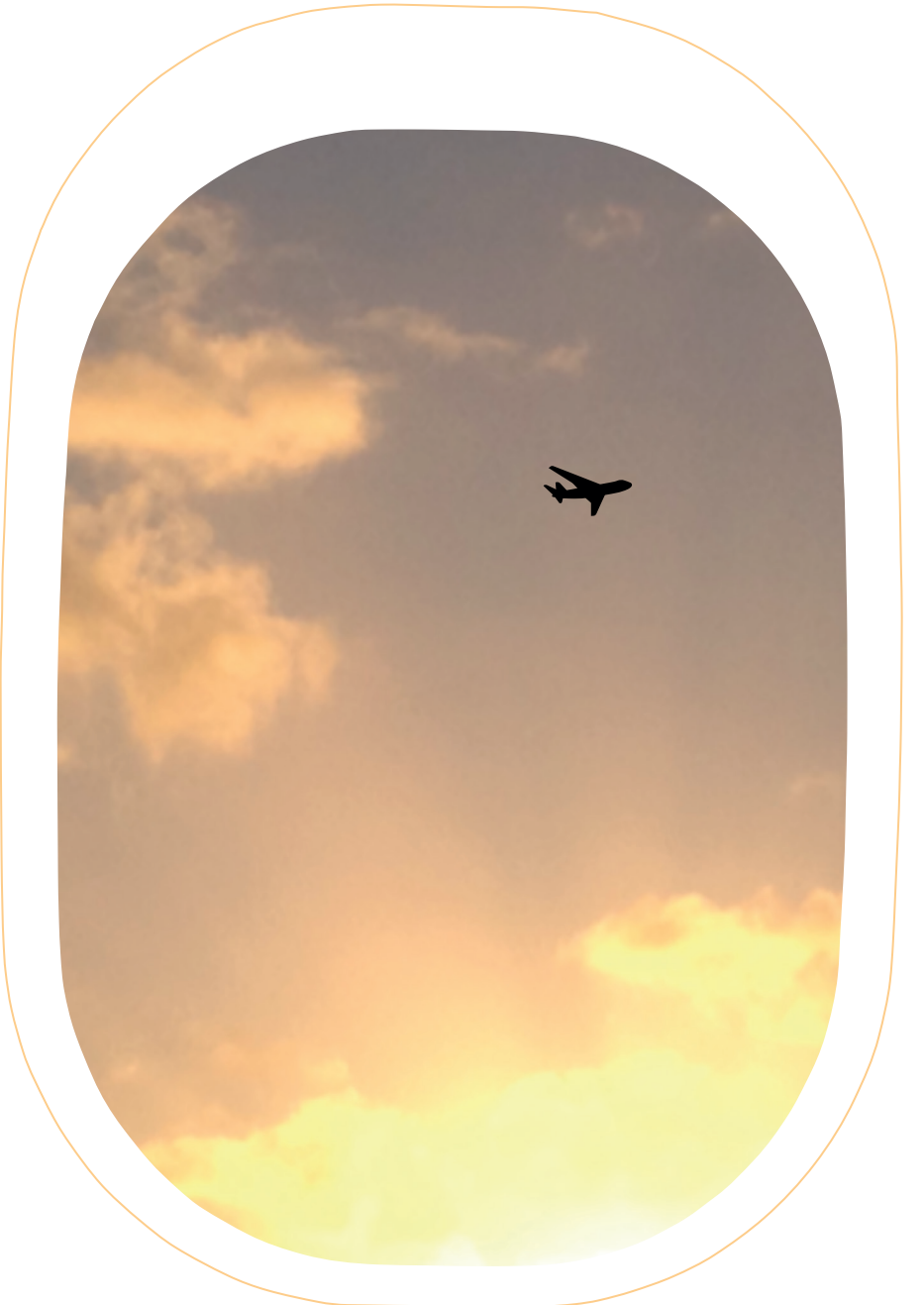

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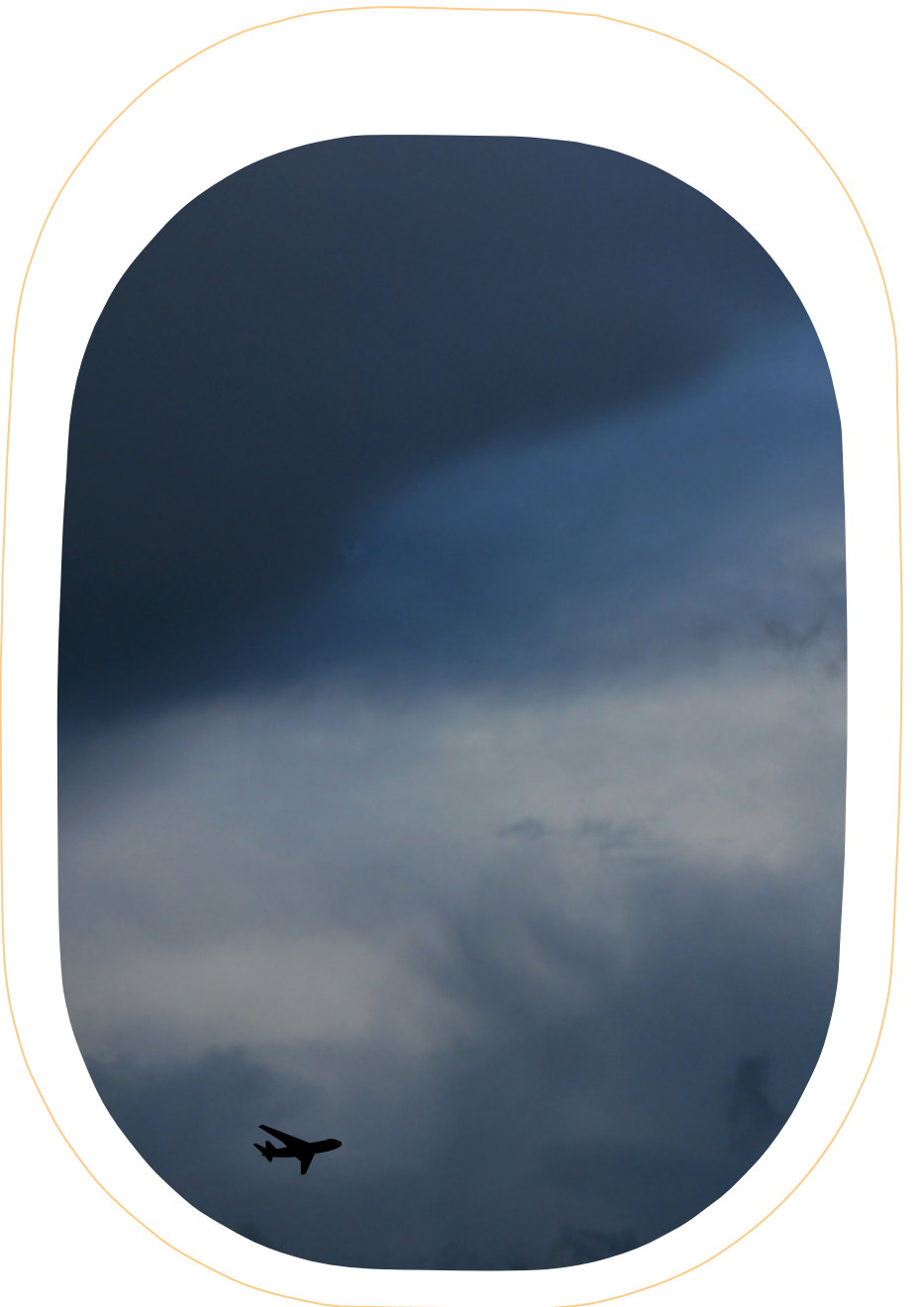

Chapter 1

General introduction

INTRODUCTION

Fear is functional. However, not all fear is realistic nor is it functional in every situation. When railroads began to be used people were afraid of their speed (Whittall 1882), but few people today can imagine that the speed of travel is in itself dangerous. Even those afraid of flying do not use speed as an argument. Travel is generally safe, and journeys undertaken at a slow tempo are not safer than those at high speed. Walking and cycling in traffic are not safer than driving a car, depending on how you make comparisons. But certainly for longer distances, if one compares the safety statistics per distance travelled, speed is more likely to be a safety-enhancing factor than a risk. From the standpoint of survival, if you have a long distance to travel it is better to use an automobile than a bicycle, and even better an airplane, if you want to arrive in one piece.

Safety is a key element of an airline service; the perception of insecurity might influence flight behaviour in general. "*An accident to an airline is like a product defect to a manufacturer, which results in lower product demand and sales revenue"* (Wong and Yeh 2003 p. 471). Besides local effects for the airline involved, accidents might in general temporarily influence passenger numbers due to a sense of insecurity regarding air travel. Wong and Yeh (2003) reported an average of 5.6% decline in passenger flow in the 2.5 months following serious accidents with rival airlines in the same Taiwanese market. Gigerenzer (2004) analysed data from the U.S. Department of Transportation and reported a 16% decline in passenger miles flown in the three months after the 911 twin tower tragedy. At the same time road traffic miles driven on interstate highways increased by 5.3%, resulting in an extra 317 road crashes with 353 fatalities. Regrettably, the act of terrorism cost 266 passengers and crewmembers (as well as many more people at the scenes of the attacks) their lives. However, the number of lives lost due to avoiding the perceived risk of flying shortly after the 911 attacks was higher than the total number of passengers and crew killed in the four fatal flights. Unfortunately, logical arguments and statistics about the safety of air travel do not assuage the fears of those suffering from aviophobia.

Assessment of anxiety disorders is based mainly on a patient's own verbal report, sometimes supported by written questionnaires. The diagnostic reliability of these assessments is a profound problem (Lang 2014). Moreover, even though physiological activation and physiological symptoms are central to these disorders, physiological measures are not used in their diagnosis (Roth 2005). Fear in general is often described in terms of physical discomfort as sweating, heart racing and muscle tension. As many as

eight out of ten symptoms experienced by individuals with aviophobia during flight are related to bodily sensations (Thyer and Himle 1987; Roth 2005). Self-report of physiological discomfort is used prominently to diagnose fear of flying, and is also often included as one of the main measures of treatment effectiveness (Van Gerwen et al. 1999). Reliance on subjective report alone may neglect important supplementary information available through psychophysiological measures, because within the domain of anxiety disorders there is a substantial discordance between subjective and physiological reactivity (Lang and McTeague 2009).

Imagine a doctor not performing a physical examination when you come to an appointment with stomach pain. You describe how you feel and the doctor asks some questions according to a standardized protocol. Does s/he have all the available information? Or would listening to the heart and lungs lead to another diagnosis? Sometimes heart failure, for example, manifests itself as a stomach problem. For an optimal diagnosis one must use all available information. Why, then, does this usually not happen in the case of anxiety disorders? Why are diagnoses nearly always based on self-report?

This thesis examines, from various angles, individual differences within a relatively large group of people with serious fear of flying (FOF) who applied for treatment to overcome this phobia. Psychophysiology is one of these angles. An important goal of this thesis is to explore added value of psychophysiological measures for the diagnosis and treatment of fear of flying. Physiological anxiety responses may augment diagnosis for this disorder, and also make it possible to track improvement during therapy. A further expectation is that measurement of physiological reactivity will lead to better prediction of treatment outcomes.

Outline of this introduction

The introduction describes a number of relevant background topics. It starts with the question of why we should trouble ourselves, and more importantly why we should bother patients, with measuring physiological variables. Then follows a review of the pros and cons of several psychophysiological measures. Next, this chapter provides general information on fear of flying and its prevalence, etiology and treatment, and concludes with an overview of the empirical studies that form the backbone of this dissertation (chapters 2 to 7).

PSYCHOPHYSIOLOGY

Lang's tripartite model states that the emotion of fear is expressed in three loosely coupled domains: affective language, overt behaviour, and physiological reactivity of the autonomic nervous system (ANS) (Lang and McTeague 2009; Lang 2014). In this dissertation, affective language is defined as self-reported data gained by use of questionnaires and structured interviews. Behaviour is not treated as an independent measure, but as a dependent measure in the empirical studies in this dissertation.

Of the three domains of the tripartite model the physiological is the least used. Analysis of psychophysiological variables is regarded as difficult for the researcher and bothersome for the patient. If indeed these variables are studied, it is mostly done in a well-controlled environment, a laboratory. And no matter how neat it is to control all disturbing variables, a lab is very different from real life. Moreover, in psychophysiological research it often happens that the participants are first year students. This makes it very difficult to generalize the results to clinical samples.

Ecologically valid research requires ambulatory measurements in naturalistic settings with real-life stressors and actual patients. Patients are people who apply for therapy and might be willing to tolerate some concurrent scientific research, but only if it does not interfere with therapeutic goals and does not become a nuisance. The participants in the research for this dissertation were highly anxious aviophobics who came for therapy. Needless to say, we did our utmost not to add procedures that would increase their anxiety. The feasibility of ANS research with these patients severely restricted our choice of physiological parameters. Measurements needed to be as non-invasive as possible, and measures needed to respond to changes in psychological state over a time scale of a few minutes. The next section, therefore, focuses on ANS functionality and the pros and cons of several measures that capture ANS activity in a naturalistic environment.

The main function of the ANS is to ensure homeostasis. It does so by responding adaptively to changes in the internal and external environment. Furthermore, the ANS can anticipatory prepare for threats to homeostasis, even in the absence of actual activity. An ANS flight-fight or freeze response can also be triggered by a phobic stressor, i.e. a subjective experience of stress without an actual objective danger present. ANS executes control by modulated activation of the sympathetic- and parasympathetic-nervous systems. Historically, a simple bipolar reciprocal model of autonomic control has been assumed, in which increased activity of one branch is associated with decreased

activity of the other. This one-dimensional model has been refined into a bivariate model of autonomic space with sympathetic activity along one axis and parasympathetic activity along the other axis, providing a multitude of combinations of sympathetic and parasympathetic activity (Berntson et al. 1994). Responses to psychological stress are highly individual, with some people showing an increase in sympathetic activity, others a parasympathetic withdrawal, and still others a combination of these responses, or even a coactivation in both branches (Quigley and Barrett 2014). On the other hand, within-individual response patterns to psychological stress seem relatively stable (Berntson et al. 1994). Non-invasive assessment of sympathetic activity and parasympathetic activity is possible by looking at the innervated organs. Heart rate variability (HRV) is the only reliable non-invasive measure currently available to capture parasympathetic reactivity. Several non-invasive measures are available to capture sympathetic reactivity.

Generally, careful consideration is needed when selecting physiological measures to capture ANS activity. Not all physiological measures capture fear intensity variations along the whole continuum. For example, Aue et al. (2012) exposed 18 spider phobic participants and 18 nonphobic participants (all female) randomly to pictures of animals (spider, snake, bird) and recorded subjective fear estimates together with several physiological measures. Skin conductance mirrored only extreme levels of fear, respiratory measures distinguished phobic from nonphobic fear but did not differentiate fear levels within phobic participants; only HR captured fear intensity variations from extremely low levels of fear to considerable phobic fear. HR seems to be a sensitive measure that captures fear intensity at both extremes of the fear continuum (Kreibig 2010; Wilhelm and Grossman 2010; Aue et al. 2012).

The heart is dually innervated. HR is the resultant of sympathetic and parasympathetic control on the intrinsic rate of the cardiac pacemaker. HR itself does not reveal the sympathetic and parasympathetic ANS cardiac activity. Different patterns of reciprocal activation, co-activation and co-inhibition in sympathetic and parasympathetic control on the heart have been found. During rest HR is tonically inhibited by parasympathetic (vagal) control, slowing the intrinsic cardiac pacemaker rate (100-150) to the normal resting heart rate of a healthy adult (60-80). Heart rate increases during inspiration and decreases during expiration, promoting an efficient exchange of oxygen in the lungs. This phasic inhibition and excitation of the heart is brought about primarily by rapid vagal control coupled to the respiratory cycle. Heart Rate Variability (HRV) in the time domain can easily be obtained from the electrocardiogram (ECG) by taking the root mean square of differences (RMSSD) in the interbeat interval between consecutive R-waves. HRV in

the frequency domain is indexed by HF (0.15 - 0.4 Hz) power obtained via spectral power analysis by fast Fourier transformation (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996; Friedman et al. 2002).

A "pure" respiratory sinus arrhythmia (RSA) can be derived when combining ECG data with respiratory signals by subtracting the shortest interbeat interval (IBI) during HR acceleration in the inspirational phase from the longest IBI during deceleration in the expirational phase (i.e., the peak-through method) (Grossman et al. 1990). RMSSD, HF power and RSA are highly correlated (Friedman et al. 2002). RSA is theoretically considered to be the soundest measure of cardiac vagal control with substantial evidence supporting its validity (Goedhart et al. 2007). Greater RSA reflects greater parasympathetic cardiac control. Higher vagal tone and greater vagal withdrawal during challenge have been associated with a greater ability to engage and disengage with environmental demands, and reduced HRV and vagal tone have been associated with anxiety and less adaptive emotion regulation (Friedman 2007; Mathewson et al. 2013; Chalmers et al. 2014).

The pre-ejection period (PEP) is a reliable and valid non-invasive measure to index changes in sympathetic cardiac control under naturalistic and ambulatory conditions (Goedhart et al. 2006). PEP is defined as the onset of the electromechanical systole (the onset of the Q wave on an electrocardiogram (ECG)) to the opening of the aortic valve (represented by the B point on an impedance cardiogram (ICG)). Shortening of the PEP reflects greater sympathetic control. Alternatives to PEP currently in use are salivary alpha-amylase (sAA), LF/HF power ratio in the frequency domain and galvanic skin response. Salivary collection is a non-intrusive measure that can be performed relatively easily in a naturalistic setting, although the procedure disrupts whatever is going on. The time lag between increased sympathetic activity and sAA secretion is unclear and may be at least 10 minutes. Salivary alpha-amylase secretion is under concurrent sympathetic and parasympathetic control and therefore cannot be used to index either input selectively (Bosch et al. 2011; Nagy et al. 2015).

The LF/HF ratio is still up for debate and seems to correlate poorly with other measures of sympathetic activity (Lien et al. 2015). A third alternative to PEP sometimes used to index sympathetic activity are electrodermal measures like skin conductance responses (or galvanic skin responses). However, electrodes are often placed on the palm of the hand, thereby restricting participants severely in their normal routines. Moreover, movement of the hand affects signal quality, thus hampering interpretation. The PEP is currently

the measure of choice in psychophysiological stress research in real life settings (Lien et al. 2015). A disadvantage of this measure is the laborious visual scoring of the entire recording. Scoring of the PEP requires identification of the onset of the Q wave, which can be ambiguous. Finally, PEP is known to be sensitive to preload and afterload effects that occur mainly during head-up tilting and changes of posture from supine to sitting to standing (Houtveen et al. 2005).

AVIOPHOBIA

Fear is a normal response to a genuine danger, anxiety a normal response to anticipated events. Fear and anxiety are not different aspects, but differ in the dimension of threat imminence (Barlow 1991). Fear and anxiety become problematic when excessive and disproportional to the actual or envisaged danger or when temporary anxiety turns into chronic anxiety. A phobia is a type of anxiety disorder, defined by persistent fear of an object or situation (American Psychiatric Association 2013). Aviophobia (fear of flying, FOF) is a persistent marked fear during or in anticipation of flying. It is disproportional to the actual danger, and this anxiety, fear or avoidance causes clinically significant distress or impairment.

Fear of flying is a heterogeneous phenomenon and often includes, or is a combination of, acrophobia, claustrophobia, fear of relinquishing control, fear of losing control over oneself, fear of a crash, and panic and social phobias (Van Gerwen et al. 1997; Oakes and Bor 2010a). Although classified as a specific phobia, also known as simple phobia, fear of flying is far from simple in view of its heterogeneous and compound nature. In general, aviophobics with agoraphobia are more concerned about panic and its consequences, whereas aviophobics without agoraphobia generally report more concern about external aspects of flying, like crashing (McNally and Louro 1992).

In the Netherlands the lifetime prevalence of anxiety disorders in the period 2007-2009 was reported to be 19.6%, and the 12-month prevalence 10.1 %, based on DSM-IV criteria. For specific phobias a lifetime prevalence of 7.9% was reported, and a 12-month prevalence of 5.0%. Between 1996 and 2007-2009 the 12-month prevalence figures did not change (de Graaf et al. 2012). The lifetime prevalence rate for a specific phobia is about half as high in men as in women (Grant and Odlaug 2015; Adolph et al. 2016), although men might underreport a specific phobia. Alcohol abuse might be a masculine masking strategy (Bekker and van Mens-Verhulst 2007). Fredrikson et al. (1996) reported

increased aviophobia as a function of age in women but not in men. It is estimated that more than a third of all people find flying difficult and distressing. Fear of flying is a debilitating disorder affecting 10% - 15% of the general population in the western world (Oakes and Bor 2010a; Ekeberg et al. 2014). Nearly all of these people either avoid flying, or fly with the help of medication, drugs or alcohol. Aviophobic people experience serious interference in daily life and social functioning due to their fear of flying.

Fear of flying is mostly an individual problem that can cause social or professional impairment (Van Gerwen et al. 1997). Besides, it reduces air travel and can have negative financial repercussions for the airline industry. A fearful passenger's failure to embark can negatively influence on-time performance, as safety regulations stipulate that luggage is not allowed to travel without its owner on board. A passenger wishing to disembark after doors have closed, or even after pushback, causes even more delay. Psychiatric issues during flight constitute 3.5% of in-flight medical incidents, most of which are caused by acute anxiety (Naouri et al. 2016).

Some studies report that people with fear of flying might be inclined to pay more for flight attributes that alleviate fear, like non-stop flights, scheduled carriers and home carriers (Fleischer et al. 2012), or pay more for flights and airlines that are perceived as safer (Fleischer et al. 2015; Koo et al. 2015). Participants in these studies did not actually book a flight or pay for their choice. To my knowledge no research on actual booking behaviour with risk/price trade-offs has been published. Empirical research on actual risk/price trade-off behaviour is needed (Savage 2012).

ETIOLOGY OF AVIOPHOBIA

Several pathways to the onset of phobia are known. The **first** is direct learning through classical conditioning of aversive events. Twelve (71%) out of 17 aviophobic participants without agoraphobia reported a threatening event during a flight (e.g. severe turbulence) as an etiological factor (McNally and Louro 1992). None of the 17 aviophobic participants with agoraphobia in the study cited exposure to threatening events as the cause of their phobia. Wilhelm and Roth (1997) reported that 17 (46%) of 37 aviophobics without a comorbid panic disorder had unpleasant (24%) and even life-threatening (22%) flight experiences. In this study, for the 21 control participants without aviophobia the numbers were 5% respectively 9%. Schindler et al. (2016) reports that 15 (50%) of 30 aviophobic participants and 16 (53%) of 30 healthy controls reported frightening events

in the air. These numbers are in sharp contrast with percentages found in an amazingly large sample of 2001 self-referred highly phobic adults who applied for a fear of flying treatment program (Nousi et al. 2008). Of all these people 85.6% flew before applying for treatment and reported uneventful flights, 5.7% flew before treatment and reported an event (5.4%) or even traumatic flight (0.3%), while 8.7% had no previous experience with flying. These numbers substantiate that direct conditioning cannot be the only mechanism in the development of fear of flying. In any case, it is unlikely that all people with a fear of flying have had a serious incident or accident; the number of these negative events is simply too low to account for the high prevalence of aviophobia. Moreover, a significant proportion of the healthy controls mentioned previously reported frightening events during flight without developing aviophobia.

The discrepancy in reported frightening events might partly be due to nomenclature. Although people with fear of flying may not have experienced flight-related incidents or accidents, they still may have thought that they were in a threatening situation. Pilots classify a discontinued approach (a "go-around"), a non-event that breaks the routine. However, unexpected roaring of the engines, pitch changes and associated acceleration, and vestibular effects might scare a passenger. A passenger can interpret a non-event as (extremely) dangerous and life-threatening and thus experience it as traumatic. A person's appraisal of a situation is the key to the resulting emotion (Frijda 1986; Lazarus 1993). Emotionally intense events tend to be remembered very well (McNally 2016). A problem in research on the conditioning of FOF is that people who develop FOF will probably remember a frightening instance associated with flight, whereas controls may have no recall of negative flight experiences; for them the experiences did not linger or result in a lasting aversion to flight. Retrospective recall might even favour remembrance of events that never occurred to explain current emotional distress (McNally 2016). Finally, individual differences in associative learning may contribute to the development of aviophobia, and explain why some individuals develop fear of flying after an aversive event associated with flying, and others do not. For example, Vriends et al. (2012) reported a slightly stronger conditioning effect to phobia-unspecific frightening pictures and frightening words among 33 aviophobic participants compared to 39 non-aviophobic control participants.

A **second pathway** to developing aviophobia is indirect learning through observation (vicarious learning, (Rachman 1977)). Published reports include a limited number of experimental studies supporting observational fear learning in toddlers and young children (see LoBue and Rakison 2013 page 286 for details), and one study with adults with

fear of flying (Schindler et al. 2016). Here 11 (37%) of 30 aviophobic participants reported that a family member or other important person suffered from past or present fear of flying. However, only two patients (6%) reported that watching somebody in their family undergoing a strong fear reaction during flight triggered their own phobia. Also familial resemblance of fear of flying may be partly attributable to a shared genetic sensitivity to anxiety disorders, the heritability of which is known to be substantial (Hettema et al. 2001).

The **third pathway** through which a fear of flying can be acquired is transmission of information and instruction (Rachman 1977). People with anxiety disorders have an attentional bias for threat cues (LoBue and Rakison 2013; Sarapas et al. 2017). These threat cues are omnipresent in the media. Aviophobic participants without agoraphobia reported significantly more often (71%) than aviophobic participants with agoraphobia (18%) that verbal and media information figured in the development of their fear of flying (McNally and Louro 1992). Schindler et al. (2016) found that a significantly higher percentage of patients with fear of flying (70%), compared to non-aviophobic controls (37%), felt influenced by media information about crashes and other flight incidents. Only three of these patients (9%) reported informational learning as triggers of their phobia; the majority of patients reported the influence of the media information after the beginning of their phobia. Informational learning might be an important factor in the maintenance of fear of flying.

A **fourth pathway** to aviophobia might be non-associative learning. This pathway to the onset of phobia is an extension of the previous three paths, with the addition that some fears are non-associative and are based on innate fear cues specific to evolutionarily threats which do not require prior association with aversive stimuli (Gray and McNaughton 2003). Fear and avoidance of certain stimuli have in the past proven beneficial to the survival of the species (Seligman 1971). A false negative fear reaction might result in death, while false positive fear reactions, in isolation, have few consequences: better safe than sorry. However, when too many false positives cumulatively begin to impair daily functioning there is a problem (Adolphs 2013). Phobias can be seen as instances of highly "prepared" learning, and the dangers natural to a species (spiders, snakes, heights) lead easily to phobia (Seligman 1971).

The four pathways do not necessarily work in isolation, although people differ in sensitivity to different pathways to develop aviophobia (Schindler et al. 2016). Individual risk factors seem to play a crucial role in the onset, development and maintenance of

anxiety. These risk factors include personality characteristics like neuroticism, a genetic vulnerability factor related to many anxiety disorders (Middeldorp et al. 2005; Smoller et al. 2008). An enhanced genetic liability can contribute to the development of anxiety disorders and specific phobias. Phobias in general are moderately heritable with an estimated heritability ranging from 20% to 40% (Hettema et al. 2001). Twin studies on the heritability of specific phobia are rare; a review by Houtem et al. (2013) included only 10 studies and found a mean heritability for specific phobias of 25%, range 0-33.
Stressful life events might enhance conditionability and increase vulnerability for developing aviophobia (Wilhelm and Roth 1997). Schindler et al. (2016), who reported that about 50% of aviophobics and controls indicated frightening events in the air, reported a significant difference between aviophobics (60%) and controls (19%) in reported stressful life events at the time of their frightening flight experience. Memory recall of distressing events appears to play a significant role in the acquisition and maintenance of aviophobia. Unexpected or inexplicable events during flight are quite common and many passengers have distressing moments during flight. Most people forget these unsettling experiences and do not develop a conditioned fear of flying in reaction to these events.

Fear is embedded in a network of causal relationships with cognitive processes. Motivation, attention and memory are part of an adaptive response to a threatening stimulus. Rumination about fear and increased expectation can be associated with increased vigilance and attention to potentially dangerous stimuli (Adolphs 2013). People generally overestimate the consequences of fearful stimuli (Seligman 1971), and people with anxiety disorders have an additional bias to rate stimuli in general as more frightening or negative (LoBue and Rakison 2013). Threat cues seem more salient to anxious individuals (Sarapas et al. 2017), and threat cues are abundant during flight. Before and during flight passengers are constantly reminded of safety and safety aids (e.g. the safety briefing before flight pointing out emergency exits and life vest locations, seat belt signs illuminated during turbulence, dimming of lights during start and landing, et cetera). The mere availability of a physical safety aid may paradoxically elicit, rather than mitigate anxiety, even more so in individuals hyper vigilant for phobic cues (Blakey and Deacon 2015).

TREATMENT OF AVIOPHOBIA

Although fear of flying is highly prevalent, only a small percentage of people with this phobia face their fear and apply for therapy. The preferred treatment method is cognitive-behavioural therapy combined with in-vivo exposure (Van Gerwen et al. 2004; Oakes and Bor 2010b; Pearl and Norton 2016). The complex and heterogeneous nature of fear of flying calls for interventions known to be effective for similar anxiety disorders. Therapy often tackles the multitude of underlying phenomena with a combination of providing information, cognitive restructuring, relaxation training and graded exposure, both in-vitro and in-vivo (Van Gerwen et al. 2004; Oakes and Bor 2010b). Imaginal exposure, virtual reality and computer-assisted exposure can be part of in-vitro exposure therapy and have comparable efficacy for fear of flying (Rus-Calafell et al. 2013). Although non-exposure treatments for specific phobia do outperform no treatment, the magnitude of their effect is only slightly greater than that of placebo versus no treatment (Wolitzky-Taylor et al. 2008). Exposure seems to be a necessary component in the treatment of aviophobia. In-vivo exposure for specific phobia yields better short-term results than imaginal exposure and virtual reality exposure (Wolitzky-Taylor et al. 2008). However, stand-alone in-vivo exposure therapy is associated with high dropout rates and low treatment acceptance (Choy et al. 2007). Cognitive interventions before exposure enable patients to take part in flight-exposure; this would not otherwise be possible (Oakes and Bor 2010b).

Most treatment facilities and programs are run in close co-operation with a domestic airline and end the treatment with a "graduation" flight. Treatment is often group-based, consisting mostly of 5 to 10 participants, and conducted over one or two days. A few facilities provide individual treatment and a number of shorter sessions if desired or required (Van Gerwen et al. 2004). Efficacy of treatment is defined as a reduction in self-reported anxiety from pre- to post-treatment, or partaking the graduation flight or a post-treatment flight. Acclaimed success rates of therapy range from 67 to 96% (Van Gerwen and Diekstra 2000; Van Gerwen et al. 2004; Oakes and Bor 2010b).

The multicomponent group-treatment for fear of flying may include therapeutic ingredients that are unnecessary for individual participants, but that favour transdiagnostic treatment gains (Deacon 2013). Comorbidity across anxiety disorders is high (Pearl and Norton 2016). Many anxiety disorders have much in common, like attentional biases, inaccurate threat beliefs, the use of safety behaviours, escape and avoidance. The multi-component transdiagnostic fear of flying treatment packages will

tackle most of these components, and might greatly improve quality of life as well as alleviate fear of flying.

CONTEXT OF THE EMPIRICAL STUDIES IN THIS DISSERTATION

Aviophobic participants in the empirical studies were individuals who applied for treatment to overcome their fear of flying. Most participants were self-referrals. Health care agencies, health care professionals and company health programs referred a minority of participants. Inclusion criteria for all studies were a good understanding of the Dutch language and no flight scheduled within 5 weeks of start of treatment. Airline personnel were excluded from the studies. Other reasons for exclusion were current use of cardioactive medication like β blockers, and pharmacotherapeutic medication. Participants followed a highly standardized treatment program for fear of flying at the VALK foundation in The Netherlands. This institution is a joint enterprise of the Section of Clinical Psychology of Leiden University with Amsterdam's Schiphol Airport and several Dutch airlines. It specializes in fear-related problems, especially fear of flying. The fear of flying treatment program starts with a thorough diagnostic assessment, including pre-treatment phobia and flight-anxiety measurements, followed by a maximum of four individual 1-hour therapeutic sessions, covering general information on factors relevant to fear and anxiety, relaxation and breathing techniques, and coping skills. Claustrophobia, acrophobia, traumatic transportation accidents and traumatic social events were addressed where applicable. Participants started a two-day cognitive-behaviour group treatment (CBGT), lasting 20 hours in total, five weeks after diagnostic assessment. CBGT groups consisted of a minimum of five to a maximum of eight participants, a therapist and an airline pilot. The first day of group treatment focused on psycho-education and technical information on flying. The second day focused on exposure and included two flights in a full motion cabin flight simulator normally used for flight safety training for cabin crew. The day ended with in vivo exposure during guided return flights of at least one hour each on a commercial airliner. Three months after CBGT participants were invited to attend an optional single three-hour follow-up session. Details of the therapeutic protocol have been published elsewhere (Van Gerwen et al. 2002, 2006). Written informed consent was obtained from all participants previous to the diagnostic process. The local medical ethics committee approved the research protocol for the studies in this thesis.

All empirical studies in this thesis were part of a longitudinal study on fear of flying, and five out of six studies utilized data from the same sample of aviophobic participants. The study described in chapter 3 utilized a different sample of aviophobic and nonphobic participants. The number of participants in the separate studies depended on the research question. Some studies required more stringent criteria than others. For example, inclusion criteria for the study mentioned in chapter 4 were complete data on all essential questionnaires at the start and at the end of treatment, in combination with complete data of all physiological variables (HR, RSA, PEP) during both flights. The security checks at the airports were a major challenge for the physiological measurements. The electrodes of the ambulatory measurement device required physical patting down of all participants. After security screening not all recording devices recorded all variables properly, a factor that excluded participants with missing data from the chapter 4 study. Nevertheless, all these participants were included in the study mentioned in chapters 6 and 7, because research questions of these studies allowed analyzing strategies that deal with partially missing data without having to exclude participants.

EMPIRICAL STUDIES IN THIS DISSERTATION

At the end of the 19th century James (1884) and Lange (1885) developed the theory that stimuli from the environment lead to physical reactions like rapid heartbeat, muscle tension, etc. Emotions are the result of sensing these reactions. With phobic people, exaggerated subjective arousal may arise from exaggerated physiological arousal during exposure to anxiety-related stimuli. On the other hand, the primary deficit in phobics may not be exaggerated physiological arousal, but a tendency to focus attention on bodily sensations and/or overinterpret these signals as danger signals. Phobic individuals may be prone to interpret normal bodily sensations in a threatening manner in this more psychological approach. **Chapter 2** examines the relationship between subjective and physiological arousal in individuals with fear of flying and controls without aviophobia when confronted with flight-related stimuli. The physiological perspective predicts a higher reactivity in phobics than non-phobics to flight-related stimuli and, within the group of phobics, a significant correlation between physiological reactivity and the amount of self-reported fear. The psychological perspective predicts a weaker concordance between subjective and physiological arousal, which may be limited to individuals who score high on anxiety sensitivity.

Chapter 3 thoroughly investigates an aspect of a relatively new treatment for aviophobia. Virtual Reality (VR) techniques are emerging for the treatment of many disorders, including phobias. An important element of VR therapy for phobic disorders is that the exposure is done gradually to more anxiety-arousing situations, with therapists continuously monitoring the anxiety level of a patient. This can be done using Subjective ratings of Anxiety (SUD), behavioral observations or physiological measures. The latter have the advantage of being more objective. However, physiological measures require a baseline measurement because of individual variation. One often-used procedure is to obtain a physiological baseline recording when the patient is placed in a neutral VR world, i.e. a VR world that should not include phobia-related stressors. Nevertheless, even without a phobia-related stressor, it is not clear whether the experience of being placed in a Virtual Environment (VE) in itself causes some level of anxiety. Chapter 3 explores whether it is possible to create a truly neutral world that causes no anxiety. This 'real' neutral world could then be used as baseline for further VR research.

Chapter 4: Anxiety sensitivity is the tendency to fear anxiety-related bodily sensations, based on the belief that the sensations have harmful consequences (Reiss 1991). Individuals with high anxiety sensitivity are prone to interpret normal bodily sensations as threatening, whereas those with low anxiety sensitivity experience these sensations as unpleasant but non-threatening. Anxiety sensitivity has been identified as a vulnerability factor for flight phobia. In this study we examined whether AS moderates the effects of somatic sensations and autonomic nervous system reactivity on flight anxiety induced by real flight. If so, this might have implications for interventions during CBT.

Some cognitive coping strategies seem more adaptive than others, while the use of certain maladaptive cognitive coping strategies has been linked to psychopathology. People with aviophobia who seek treatment are found to have a dispositional tendency to use maladaptive strategies, including avoidance behaviour, to cope with their anxiety. Almost no studies of anxiety problems have been performed to find whether psychological interventions may change the use of specific coping strategies, and if so, whether these changes predict subsequent reductions in anxiety. **Chapter 5** describes research with aviophobic participants who were followed from pre-treatment to long-term follow-up, 41 months later. We expected that participants, who at the start of treatment, more often used maladaptive strategies than adaptive strategies would profit less from treatment. Furthermore, we expected that targeted interventions during CBT would reduce the predominant use of maladaptive strategies and enhance the use of more adaptive coping strategies. Finally, we hypothesized that in particular a reduction

of the maladaptive coping style during treatment would predict a better long-term therapy outcome.

Next to cognitive interventions, exposure is the second basis of cognitive behavior therapy. According to emotional processing theory, exposure to a feared stimulus activates a 'fear network', and activation of this fear network is seen as a necessary condition for improvement of phobias and other anxiety disorders. Successful emotional processing during exposure is subsequently indicated by within-session and between-session habituation of fear responses. **Chapter 6** deals with the question of whether fear activation and habituation during exposure are predictive of short-term and long-term therapy results. A second goal was to see whether the prediction of therapy outcome would be improved by adding measurements of physiological reactivity to self-reporting of anxiety.

Chapter 7: The tripartite model of Lang (2014) states that the emotion of fear is expressed in three loosely coupled domains: affective language, overt behaviour, and physiological reactivity. Emotion can be seen as the organizing process that coordinates these different systems to prepare the individual for optimal and effective response to challenges. When the individual is faced with increasing demands the coordinated co-activation of multiple response systems would seem even more important. Response coherence would thus be expected to increase with increasing emotional intensity. Conversely, adaptive emotional functioning could be indicated by proper and progressive response coherence upon increasing demands. If so, the magnitude of coherence could be an indication of progress during therapy. In this study we first examined whether synchronous change in subjective and physiological reactivity over repeated exposures increased from watching a flight video (low intensity) through simulated flight (medium intensity) to actual flight (high intensity). Second, we assessed whether the magnitude of synchronous change predicted short- and long-term treatment outcome. Based on the assumption that successful treatment of anxiety disorders should be indicated by synchronous change, we expected participants with more synchronous change in the two response systems during treatment to show lower flight anxiety at the end of treatment and three years after treatment than participants with less synchronous change during treatment; we also expected them to have engaged in more actual flights.

Finally, **chapter 8** summarizes and discusses the main findings and their clinical implications, and presents directions for further research.

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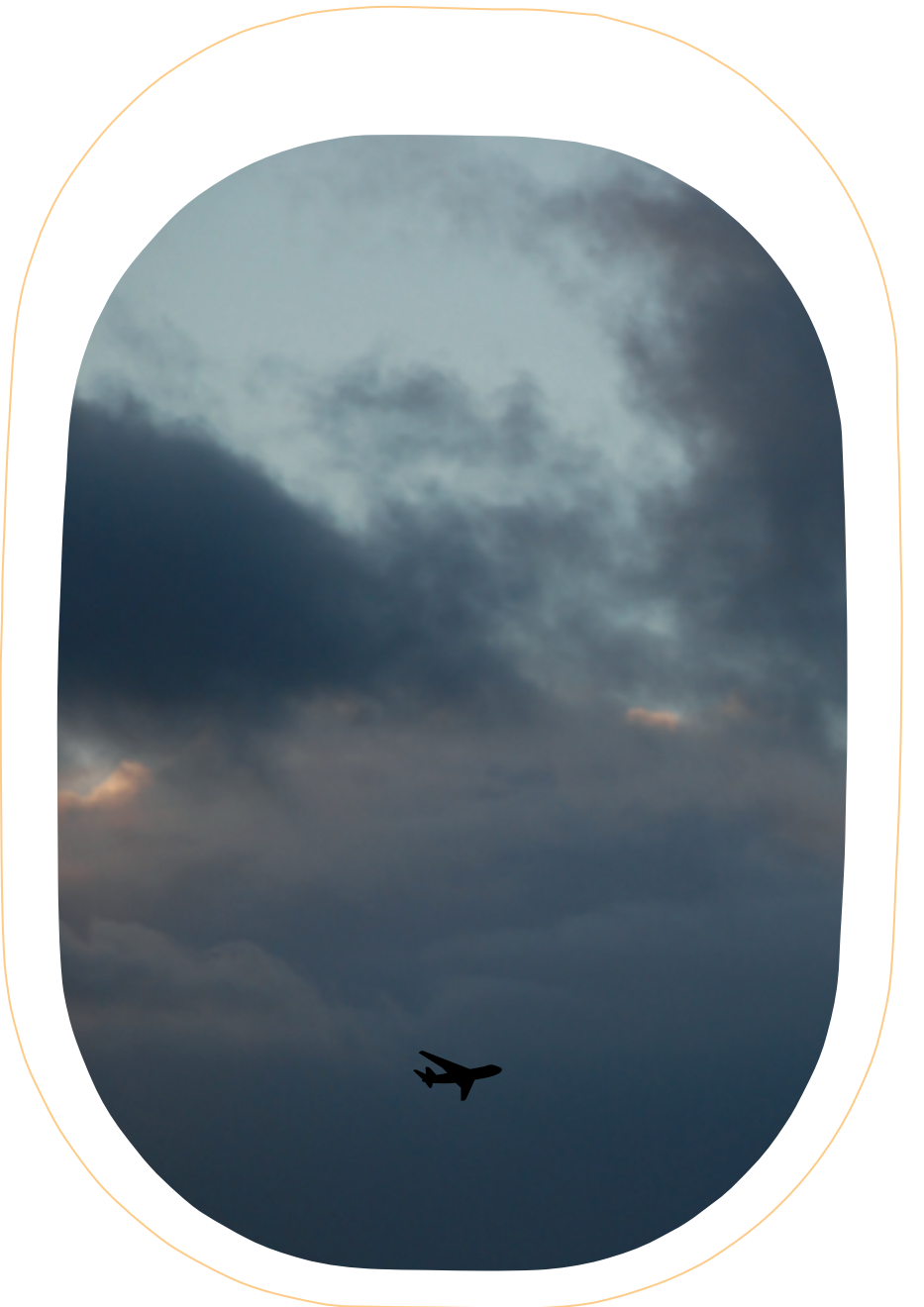

Chapter 2

Physiological reactivity to phobic stimuli in people with fear of flying

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ABSTRACT

Objective: The nature of the relationship between physiological and subjective responses in phobic subjects remains unclear. Phobics have been thought to be characterized by a heightened physiological response (physiological perspective) or by a heightened perception of a normal physiological response (psychological perspective).

Method: In this study we examined subjective measures of anxiety, heart rate and cardiac autonomic responses to flight-related stimuli in 127 people who applied for fear of flying therapy at a specialised treatment centre and 36 controls without aviophobia.

Results: In keeping with the psychological perspective, we found a large increase in subjective distress (η^2 = .43) during exposure to flight-related stimuli in the phobics and no change in subjective distress in the controls, whereas the physiological responses of both groups were indiscriminate. However, in keeping with the physiological perspective we found that, within the group of phobics, increases in subjective fear during exposure were moderately strong coupled to heart rate (r=.208, p=.022) and cardiac vagal (r=.199, p=.028) reactivity. In contrast to predictions by the psychological perspective, anxiety sensitivity did not modulate this coupling.

Conclusion: We conclude that subjective fear responses and autonomic responses are only loosely coupled during mildly threatening exposure to flight related stimuli. More ecologically valid exposure to phobic stimuli may be needed to test the predictions from the physiological and psychological perspectives.

INTRODUCTION

The prevalence of people with varying degrees of fear of flying is estimated at 7-40% of the general population in industrialized countries (1, 2). Curtis (3) reports a lifetime prevalence of 13.2% of people who are impaired by fear of flying, while Depla (4) mentions that 6.9% of all people experience serious interference in daily life and social functioning due to fear of flying. In view of recent events like the 9/11 bombing this percentage is not expected to decrease. Although distinguished by their fear of flying from other types of phobics, flying phobics are a heterogeneous group. Fear of flying can be the manifestation of one or more other phobias, such as claustrophobia or social phobia. It can also be the effect of generalization of one or more natural environment phobias, such as fear of heights, falling, storms, water, instability, et cetera. Fear of losing control and a high need to have control over a situation is often associated with fear of flying (1, 5-7).

As much as eight out of ten symptoms experienced by individuals with specific phobias during exposure to a phobic stimulus might be related to bodily sensations (8, 9). This applies in full to aviophobia where physiological sensations is one of the major symptoms reported. Physiological discomfort is used prominently in the diagnosis fear of flying, and it is often invoked as one of the main measures of treatment effectiveness (10). In spite of the importance of physiological sensations in fear of flying, many studies on aviophobics evaluate these sensations exclusively by verbal report. This might be problematic, as the relationship between self-reported feelings of anxiety and actual physiological reactivity has proven to be complex (11-21).

Two distinct theoretical perspectives have been proposed. In the physiological perspective, a historical extension of the original formulation by James and Lange (22, 23), exaggerated subjective arousal is thought to arise from exaggerated physiological arousal during exposure to anxiety-related stimuli. Increased sympathetic and decreased parasympathetic nervous system activity is sensed through afferent feedback from the affected organs (sweat glands, heart, lungs) and causes anxiety (24-29). In the psychological perspective, the primary deficit in phobics is not exaggerated physiological arousal, but a tendency to focus attention on bodily sensations and/or overinterpret these signals as danger signals. In this perspective, and combining both viewpoints, anxiety sensitivity is seen as a key moderator between the experience of bodily sensations and anxiety (30, 31). Anxiety sensitivity is the fear of anxiety related bodily sensations, based on the belief the sensations have harmful somatic, psychological or social

consequences (32). Individuals with high anxiety sensitivity are prone to interpret normal bodily sensations in a threatening manner whereas those with low anxiety sensitivity experience these sensations as unpleasant but non-threatening. Anxiety sensitivity is believed to be a dispositional variable distinguishable from trait anxiety (33).

To study the divergent predictions as derived from the physiological and psychological perspective simultaneous assessment of subjective and physiological responses during exposure to phobic stimuli is needed. To date surprisingly few studies have simultaneously assessed the changes in subjective fear levels during exposure to simulated or real flights in aviophobics together with physiological reactivity. These studies usually recorded increases in heart rate (HR) and respiration rate or decreases in heart rate variability (HRV), a measure of cardiac parasympathetic control, as the main physiological outcome variables. Using heart rate, for example, Beckham (34) found high levels of synchrony over time between physiological arousal and subjective anxiety during flight exposure. Synchrony over time even exhibited prognostic value for positive treatment outcome in their study. Contrasting results were obtained in a randomized double blind placebo design by Wilhelm and Roth (35). They tested the effect of alprazolam (a benzodiazepine) during two flights in women suffering from fear of flying. During the first flight, alprazolam significantly reduced anxiety compared to placebo, whereas HR was in fact higher. On the second flight, without alprazolam, women that had been on alprazolam had both higher levels of self-reported anxiety and higher levels of HR, whereas the women that had been on a placebo had lower levels of self-reported anxiety together with a nearly significant decrease of HR. Bornas et al. (36) compared 4 groups of psychology students, selected for low or high scores on a fear of flying questionnaire and either low or high HRV levels during a baseline measurement. Low HRV fearful flyers reported higher levels of anxiety than any other group when confronted with flight-related pictures and sound, while high HRV fearful flyers did not report higher levels of anxiety than controls. Finally, Ekeberg et al. (37, 38) used catecholamines rather than HR or RSA as their main variable to index physiological reactivity in flight phobics. They too reported only low correlations between the psychological and physiological response to flight phobia stress (21). Taken together, the extant studies suggest that subjective report and physiological reactivity are often not in synchrony.

In the present study we re-examine the relationship between subjective and physiological reactivity in individuals with fear of flying when confronted with flight-related stimuli. We first compared phobics to non-phobic controls to test whether the physiological reactivity of the phobics, in parallel to their larger subjective reactivity,

was larger than that of non-phobic controls. Secondly, we assessed the concordance between self-reported anxiety and physiological markers of anxiety within a relatively large group of people who applied for fear of flying therapy at a specialized treatment centre. Thirdly, we investigated whether the association of self-reported anxiety and physiological markers of anxiety was moderated by individual differences in anxiety sensitivity. The physiological perspective predicts a higher reactivity in phobics than non-phobics to flight-related stimuli and, within the group of phobics, a significant correlation between physiological reactivity and the amount of self-reported fear. The psychological perspective predicts a weaker concordance between subjective and physiological arousal, which may be limited to individuals who score high on anxiety sensitivity. We extend the work in previous studies, which focused on heart rate and measures of parasympathetic activity, by adding the Pre-Ejection Period (PEP), a measure of sympathetic nervous system activity. Our focus on cardiac parameters reflects two major considerations: measurements needed to be as non-invasive as possible and they needed to respond to changes in psychological state over a time scale of a few minutes. The PEP and RSA (respiratory sinus arrhythmia, a measure of parasympathetic control) measures are uniquely qualified to meet both demands (39, 40).

METHOD

Participants

Participants were phobics that applied for therapy at the VALK foundation during the research period and non-paid volunteers without fear of flying who acted as a control sample. The VALK foundation is a facility that specializes in treating flying phobics. It is a joint enterprise of the Department of Clinical, Health and Neuropsychology at Leiden University, KLM Royal Dutch Airlines, Transavia Airlines and Amsterdam Airport Schiphol. Most people who apply for treatment at this facility are self-referrals, although lately more and more patients are referred by health care agencies, health professionals and company health programs.

During the recruitment period, 210 phobic clients who applied for treatment received written information regarding the present study at their home address a few weeks before their first visit. Out of this group, 142 were considered eligible for the study. The largest group of clients (N=27) was excluded because they were airline personnel (both cabin and flight deck crewmembers). Other reasons for exclusion were unwillingness to participate in physiological recordings (N=17), a scheduled flight within the two

weeks after recruitment (N=8), lack of time (N=5), no aviophobia (N=3), current use of cardioactive medication like ß-blockers (N=3). Another 15 clients were excluded from analyses because of equipment failure during physiological recordings. This left 127 phobic clients (57 men) with an average age of 40.5 (SD=11.0), who fulfilled the DSM-IV criteria for specific situational phobia furnishing usable data.

In the same period 39 non-paid volunteers without fear of flying and an average age of 43.4 (SD=13.5) successfully completed a part of the same protocol. Volunteers were recruited through the social network of the research institution's staff. Healthy subjects were matched with the sample of patients on age and sex. Three of them received a positive diagnosis for aviophobia during the intake and were excluded. The final 36 non-phobics (17 men) had flown at least several times; most of them had flown within 18 months of the experiment. Two subjects made their last flight 2 years before the experiment, one subject had not flown for 10 years. None of the control subjects was ever treated for fear of flying. Before start of the experiment informed consent was obtained from all participants. The research protocol has been approved by the local medical ethics committee.

Procedures

All measurements took place at the VALK facility. Upon arrival clients and control subjects were informed about the procedure. It was emphasized that participating was voluntary and neither participation nor refusal to participate impacted on the quality of treatment. After informed consent was given, six electrodes were attached and connected to the Vrije Universiteit Ambulatory Monitoring System (VU AMS) which records the thorax impedance and the ECG in freely moving subjects as described in detail elsewhere (39-43) Subjects were then seated upright and partook in three experimental conditions, always in the same fixed order. Subjects first watched a neutral video for six minutes, followed by a flight video of the same length. The flight video consisted of a flight safety demonstration video of a Boeing 747 with sound followed by some video shots of a landing Boeing 737, without sound. This video was followed by a recovery period of six minutes in which subjects were asked to relax and read a magazine. From the start of the video presentation to the end of the recovery period subjects were left alone in the experimental room. Subjective units of distress (SUD) were measured at four discrete moments: before the start of the experiment, directly after both video presentations and at the end of the recovery period. Subjects were prompted to fill out SUD's by text messages on the television screen.

Next, subjects were taken to a different experimental room and administered VALK's regular battery of questionnaires used for diagnostic purposes on fear and phobias and fear of flying in particular. Some paper and pencil questionnaires were added especially for this experiment. Finally, in a semi structured interview by a fully qualified psychotherapist, more information was gathered about flying behaviour, life events and other relevant information. Thereafter, the electrodes and the ambulatory recording device were removed.

Physiological recordings

The three target variables were HR, PEP and respiratory sinus arrhythmia (RSA). The PEP is considered a measure of sympathetic cardiac control (44) whereas RSA is a measure of parasympathetic control (45). Scoring of these variables from thorax impedance and the ECG is described in detail elsewhere (39, 42). Briefly, from the ECG (sampling rate 1000 Hz) the HR was obtained from the time between two adjacent R waves. PEP was defined from the ECG and ICG as the time interval from the Q-wave onset, the onset of the electromechanical systole, to the B-point (from the ICG), which signals opening of the aortic valves (40,44). RSA was obtained from the ECG and respiration signals by subtracting the shortest IBI during HR acceleration in the inspirational phase from the longest IBI during deceleration in the expirational phase (i.e. the peak-through method) (46). When no phase-related acceleration or deceleration was found, the breath was assigned a RSA score of zero. Automatic scoring of PEP and RSA was checked by visual inspection of the impedance and respiratory signal from the entire recording.

Using a visual display of the output of an inbuilt vertical accelerometer, we identified 3 artefact free periods that lasted at least 5 minutes each: neutral video presentation, flight video presentation, and recovery after the video presentation. Average HR, PEP, and RSA was determined across each of these periods.

QUESTIONNAIRES

All questionnaires were administered in the Dutch language.

FAS

The Flight Anxiety Situations (FAS) questionnaire was used to assess the degree of anxiety experienced in different flying related situations on a 5-point Likert-type scale, ranging from 1 (no anxiety) to 5 (overwhelming anxiety). The 32 item self-report inventory consists of three subscales: (a) an Anticipatory Flight Anxiety Scale, containing 14 items that

pertain to anxiety experienced when anticipating a flight, (b) an In-Flight Anxiety Scale, containing 11 items measuring anxiety experienced during a flight and (c) a Generalized Flight Anxiety Scale, containing seven items assessing anxiety experienced in connection with airplanes in general. The psychometric properties of the Dutch FAS proved to be excellent (10, 47). The internal consistency of the subscales of the FAS in the present study was good to excellent, Cronbach's Alpha ranging from 0.86 to 0.98

FAM

The Flight Anxiety Modality (FAM) questionnaire was used to assess the symptoms by which flying related anxiety was expressed. Each symptom is rated on a 5-point Likert-type scale, ranging from 1 (not at all) to 5 (very intensely). The 18 item self-report inventory consists of two subscales: (a) a Somatic Modality scale, pertaining to physical symptoms and (b) a Cognitive Modality scale, related to the presence of distressing cognitions. The psychometric properties of the Dutch FAM proved to be good to excellent (10, 47). The internal consistency of the two subscales of the FAM in the present study was good, Cronbach's Alpha respectively 0.89 and 0.88.

VAFAS

The Visual Analogue Flight Anxiety Scale (VAFAS) was used to examine to what extent subjects were anxious about flying. The one-tailed scale ranges from 0 (No flight anxiety) to 10 (Terrified or extreme flight anxiety) (10).

SUD

The Subjective Units of Discomfort (SUD) scale was used to examine to what extent subjects were feeling anxious at several moments. Subjects had to indicate their perceived anxiety on a scale from 1 (totally relaxed) to 10 (extremely anxious) (48).

ASI

The Anxiety Sensitivity Index (49) was used to assess fear of anxiety related symptoms. It is a 16 item self-report questionnaire designed to measure the dispositional tendency to fear the somatic and cognitive symptoms of anxiety. The items are rated on a 5-point Likert-type scale, ranging from 0 (very little) to 4 (very much). The ASI scale consists of 3 subscales: (a) AS physical concern, (b) AS cognitive concern, and (c) AS social concern. The instrument's psychometric properties and predictive values are good (50, 51). In the present study only the subscale for physical concern and the overall ASI total score were used. The internal consistency of both scales in the present study was good, Cronbach's Alpha respectively 0.88 and 0.87.

Data analysis

Comparison of phobic and non-phobic control subjects on sociodemographic characteristics and the FAS/FAM/VAFAS scales were performed with one-way ANOVA or a χ^2 tests where appropriate. Of the physiological variables, RSA had to be log (ln) transformed to obtain normal distributions. Due to scheduling conflicts only a part of all non-phobic control subjects partook in the neutral video condition (all completed the flight video and recovery conditions). We used MIXED ANOVA as our main analysis strategy in the comparison of controls and phobics. MIXED ANOVA deals with the partial missing data without having to exclude subjects. In the ANOVA on SUD scores, sex, group (phobic, non-phobic), and condition (entrance, video-neutral, video-flight, and recovery) were the fixed factors. In the ANOVA on RSA, PEP, and HR, sex, group (phobic, non-phobic), and condition (video-neutral, video-flight, and recovery) were the fixed factors.

To see whether there were concordant changes in self-reported anxiety and the physiological markers of anxiety within the group of phobics, we created two reactivity scores for each of the three physiological variables that reflected the response to the flight video (flight video – neutral video) and the extent of recovery after the flight video (flight video – recovery). We then used these reactivity scores in multiple regression analyses to predict the increase in SUD values from the neutral-video to the flight-video condition and the decrease in SUD values from the flight-video to the recovery condition, after correcting for age and sex. Anxiety sensitivity measures and the product of anxiety sensitivity with the change scores for RSA, PEP and HR were added to the regression models to test for an interaction between anxiety sensitivity and physiological reactivity. All independent variables were centered to eliminate multicollinearity problems.

RESULTS

Sociodemographic characteristics phobics and controls

Table 1 shows the sociodemographic characteristics for the group of phobic clients and the control group. Both groups did not differ significantly on sociodemographic characteristics, but control subjects had made significantly more flights than phobic subjects. As shown in table 2, scores on the VAFAS scale and all FAS and FAM (sub)-scales for both groups were reasonably in line with the established norms for these questionnaires (47). Controls had slightly lower scores than reported for a sample of 1012 non-phobic healthy controls, but the flying phobics had almost the same means and standard deviations as reported for subjects with aviophobia (47). Significant group

differences were found in the expected direction for the VAFAS and all FAS/FAM subscales. Eta square (η^2), being the effect size statistic for one-way ANOVA showed a large effect for all measures. By convention, η^2 of .01, .06 and .14 are interpreted as small, medium and large effect sizes, respectively.

Table 1. Number of participants, sociodemographic characteristics, and flight experience for the group of phobic clients and the control group.

	Controls Mean (SD or %)	Phobic clients Mean (SD or %)
Number of participants		
- total	36	127
- men	17 (47.2%)	57 (44.9%)
- women	19 (52.8%)	70 (55.1%)
Age (years)		
- total	43.4 (13,5)	40.5 (11.0)
- men	44.5 (12,7)	42.3 (9.8)
- women	42.4 (14,4)	39.0 (11.7)
Health		
- Body Mass Index (kg/m^2)	23.3 (2.3)	24.3 (3.3)
- Sports hours per week	3.4 (2.5)	2.6 (2.4)
Education		
- basic	1 (3%)	5 (4%)
- low	8 (22%)	39 (31%)
- medium	10 (28%)	13 (10%)
- high	17 (47%)	69 (54%)
Employment		
- self-employed	7 (20%)	26 (21%)
- paid employment	22 (61%)	86 (68%)
- school/study	3 (8%)	2 (2%)
- without paid work	4 (11%)	12 (9%)
Flight experience		
- never flown	0	7 (5.6%)
- flew within previous year	27 (75%)	33 (26.0%)*
- average number of flights	68.9 (91,8)	21.6 (33.0)*

* Phobics differ from controls at p<.001 (two tailed).

Table 2. Measures of flight-related anxiety and somatic complaints for flight phobics and control subjects.

	Controls N=36		Phobic clients N=127		
	Mean	SD	Mean	SD	Effect Size η^2
FAS					
Anticipatory anxiety	12.5	1.8	41.9*	10.2	.65
In-flight anxiety	12.2	2.8	35.4*	9.6	.56
Generalized flight anxiety	7.11	.47	12.7*	4.7	.24
Sum score	35.1	5.2	100.0*	21.8	.66
FAM					
Somatic complaints	11.7	1.2	26.0*	9.1	.36
Cognitive complaints	8.1	1.9	23.1*	7.3	.49
VAFAS	.56	.74	7.8*	1.4	.86

* Phobics differ from controls at p<.001 (two tailed).

Self-report data phobics and controls

A significant group by condition interaction was found for self-reported distress ($F(3, 355) = 7.74$, $p < .001$), together with a main effect of group ($F(1, 496) = 49.83$, $p < .001$). In figure 1 it can be seen that the phobics had higher levels of fear throughout, and that the interaction with condition was driven by a selective increase in SUDs in the phobics group during the flight video ($\eta^2 = .43$). A significant main effect of sex was found with female subjects (mean SUD 2.77) reporting higher levels of fear than male subjects (mean SUD 2.28) ($F(1, 596) = 5.04$, $p < .05$), but sex did not interact with group or condition.

Physiological data phobics and controls

In contrast to the substantial group by condition effect in subjective responses, no significant group by condition interactions were found in any of the three physiological variables. In fact there was no significant main effect of condition in either group. Significant main group effects did emerge for overall RSA and PEP levels. Phobic subjects had significantly shorter PEP values than controls, indicating higher cardiac sympathetic control [$F(1, 377) = 9.85$, $p < .01$], and significantly longer RSA values, indicating higher parasympathetic control [$F(1, 326) = 5.04$, $p < .05$). Average HR for the phobic subjects was not significantly higher than that of controls in all conditions. Table 3 shows average HR, RSA and PEP for the three conditions, together with the average level across all conditions in both groups.

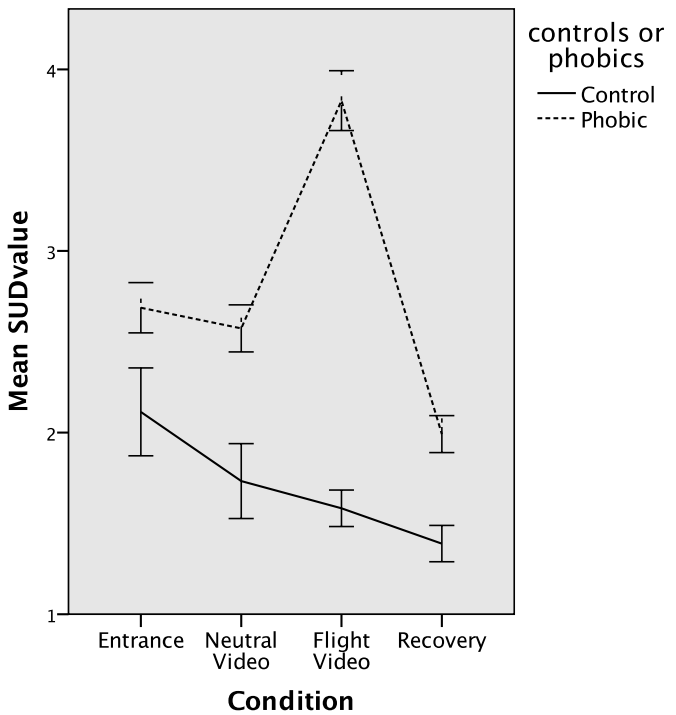

Figure 1. Mean subjective distress for flight phobics and control subjects at entrance and in response to the three experimental conditions. Error bars represent 1 standard error of the mean.

Correlations between SUD reactivity and physiological reactivity

Although the average physiological reactivity from the neutral video to the flight video was close to zero, inspection of the distribution of the reactivity scores showed striking individual differences as illustrated for RSA and HR reactivity to the flight video in figure 2. In response to the phobic stressor some subjects showed the expected decreases in parasympathetic activity whereas others showed an unexpected *increase* in RSA. These individual differences were most pronounced in the phobic group.

In the phobic group, the changes in HR and RSA were significantly correlated to the increase in SUD values from the presentation of the neutral-video to the flight-video such that increased fear was accompanied by a parallel increase in HR (r=.208, p=.022) and decrease in RSA (r=-.199, p=.028). This modest coupling was lost during recovery, however, and no significant correlation was found between the decrease in anxiety from

Table 3. Mean and SD of the three physiological variables HR, RSA, and PEP for flight phobics and controls during the three experimental conditions.

Variable	HR		RSA		PEP	
Condition	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Neutral Video						
Controls	69.2	9.8	37.6	27.2	116.3	16.6
Phobics	71.6	11.8	49.9	31.0	112.7	19.8
Flight Video						
Controls	69.1	9.5	42.3	22.0	124.6	16.8
Phobics	71.4	11.1	48.7	25.9	114.5	21.2
Recovery						
Controls	69.4	9.4	42.9	21.4	124.2	17.6
Phobics	72.3	10.8	48.3	26.1	113.3	21.6
Overall						
Controls	69.2	9.4	41.0	21.9	121.4	17.2
Phobics	71.7	11.2	49.0*	26.6	113.4**	20.8

Phobics differ from controls at * p<.05 and ** p<.01 (two tailed).

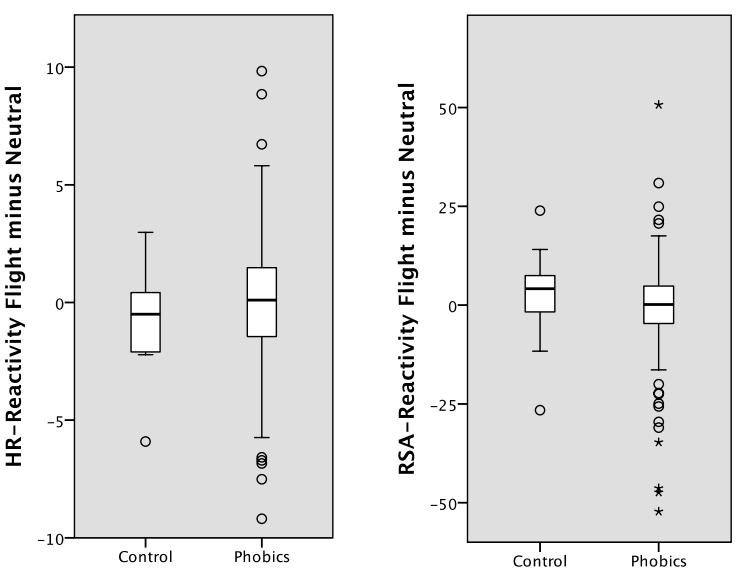

Figure 2. Box plots of HR and RSA reactivity to the flight video for flight phobics and control subjects.

the flight-video to the recovery period and the parallel changes in HR, RSA, or PEP during this same time interval. Control subjects showed no correlations at all between the SUD reactivity and physiological reactivity scores.

Regression Analysis

Multiple regression analyses were performed to test the hypothesis that phobics who score high on anxiety sensitivity in combination with a heightened physiological reaction to flight stressors show a concordant higher increase in self-reported anxiety when confronted with these stressors. For the operationalisation of AS we used both the total score on the ASI and the physical concern subscale, thereby maximizing the possibility to find a relationship between changes in self-reported distress and a physiological marker of anxiety. Because only neutral to flight reactivity was significantly associated with SUDs, we proceed with the regression analyses limited to this reactivity only.

Physiological reactivity, anxiety sensitivity and their interaction did not significantly predict the increase in self-reported anxiety from the neutral to the flight video for the phobic subjects, although the interaction of ASI physical concern subscale with PEP-reactivity nearly reached significance ($r=-.21$, $p<.07$). Overall, flight phobics who are afraid of anxiety related bodily sensations did not report more distress than phobics who score low on this trait, even when they show stronger physiological responses.

DISCUSSION

This study examined the effects of flight-related stimuli in a relatively large sample of aviophobics and a control group without fear of flying. Both subjective measures of anxiety and cardiac autonomic responses were recorded. Results indicate that strong subjective fear responses in flight phobics may be induced by exposure to flight related stimuli without the typical increase in sympathetic and decrease in parasympathetic activity seen during the classical 'fight-flight' response. However, the patterning of cardiac parasympathetic reactivity did predict increases in distress during the flight video. Specifically, phobics with the lowest increase in subjective distress were characterized by an increase in RSA and decrease in HR, whereas the phobics with the highest increase in subjective distress showed a decrease in RSA and increase in HR. These findings add to the many studies which have shown that the relationship between self-reported feeling of anxiety and physiological reactivity to stressors is complex (11-19, 19, 19-21, 35, 52-53).

The strong variation in the direction of cardiac parasympathetic reactivity, shown in figure 2, is intriguing and could reflect more than just a random fluctuation against a mean reactivity of zero. Indeed, our RSA data are strongly reminiscent of similar data in dental phobics presented by Bosch et al. (54, 55), who found that exposure to a video with dental surgery invoked an average increase in RSA rather than a decrease, with large individual differences in the direction and the magnitude of the RSA response found there too. Increased parasympathetic activity was seen in blood phobics as well, (56) although the effect was relatively minor (57). We suggest that exposure to phobic stimuli is a complex stressor in that it can invoke both fight-flight responses, characterized by increased sympathetic and reciprocal decreased parasympathetic activity, as well as a passive coping response (freeze) characterized by increased sympathetic activity paired to *increased* parasympathetic activity.

Taken together, these findings do not confirm the usual prediction made from the physiological perspective in which the subjective fear response is thought to reflect feedback from the increased fight-flight responses generated by fear circuits in the brain (hippocampus- amygdala- hypothalamus). Only 4% of the increased fear during the flight-video was explained by a physiological factor. At the same time our results also do not unequivocally support the psychological perspective that argues that during exposure to phobic stimuli, the ongoing physiological signals get more attention, and are overinterpreted as danger signals (12, 33, 58-61). Specifically, we could not confirm the hypothesized effects of anxiety sensitivity that are part of the psychological perspective. Flight phobics who are afraid of anxiety related bodily sensations (high ASI-total and high ASI-physical concern) did not report a stronger increase of distress than phobics who score low on this trait, even when they showed the typical fight-flight response.

Averaged across all experimental conditions, i.e. even during neutral and recovery periods, phobics as a group reported increased anxiety levels compared to controls, which was coupled to lower baseline levels of PEP and higher RSA. This pattern of increased sympathetic activity paired to increased parasympathetic activity may be evoked by the sheer anticipation of exposure to phobic stimuli, while recovery from this effect seems to be delayed. A potential explanation for the increased (anticipatory) anxiety, which honours both physiological and psychological contributions, might be found in a larger interoceptive awareness at baseline in phobics than in controls. Generally, interoceptive awareness, for instance operationalised as heart beat perception, is not very accurate (62) and most people underestimate their heart rate (63, 64). Accurate perception is, however, slightly more prevalent among panic disorder patients and people with accurate

perception have higher anxiety sensitivity scores (62). This may be related to the specific pattern of parasympathetic activation and sympathetic co-activation evident in baseline PEP and RSA of the phobics, which may result in a more forceful contraction of the heart that is known to increase the ease of heart beat perception (62, 65, 66).

A major limitation of this study is the low ecological validity of the stimuli used. The video stimulation may simply not have elicited sufficient emotional reactions. In other studies with generalised anxiety disorder patients, aviophobics, and dental phobic patients the uses of video scenes to evoke psychophysiological reactions have been proven to be effective (11, 14, 16, 67-73), but Bornas et al. (36) who used pictures instead of videos reports that the addition of sound might be crucial to elicit proper physiological reactions. They found different reactions to pictures with and without sound within sub samples of flying phobics and non-phobics. Here, we used an exposure video comprised of a flight safety demonstration with sound followed by three video shots of a landing airplane without corresponding sound and this may have attenuated physiological reactivity. Future research could benefit from stimuli that resemble the feared object better.

In conclusion we find that subjective fear responses and autonomic responses are only loosely coupled during mildly threatening exposure to flight related materials. A relatively large discrepancy was found in subjective distress during exposure to flight-related stimuli between phobics and controls, whereas the physiological responses of both groups were indiscriminate, which argues in favour of the psychological perspective. In keeping with the physiological perspective, however, we find that, within the group of phobics, increases in subjective fear during exposure are moderately strong coupled to heart rate and cardiac vagal reactivity. More ecologically valid exposure to phobic materials may be needed to more robustly test the predictions from the physiological and psychological perspectives.

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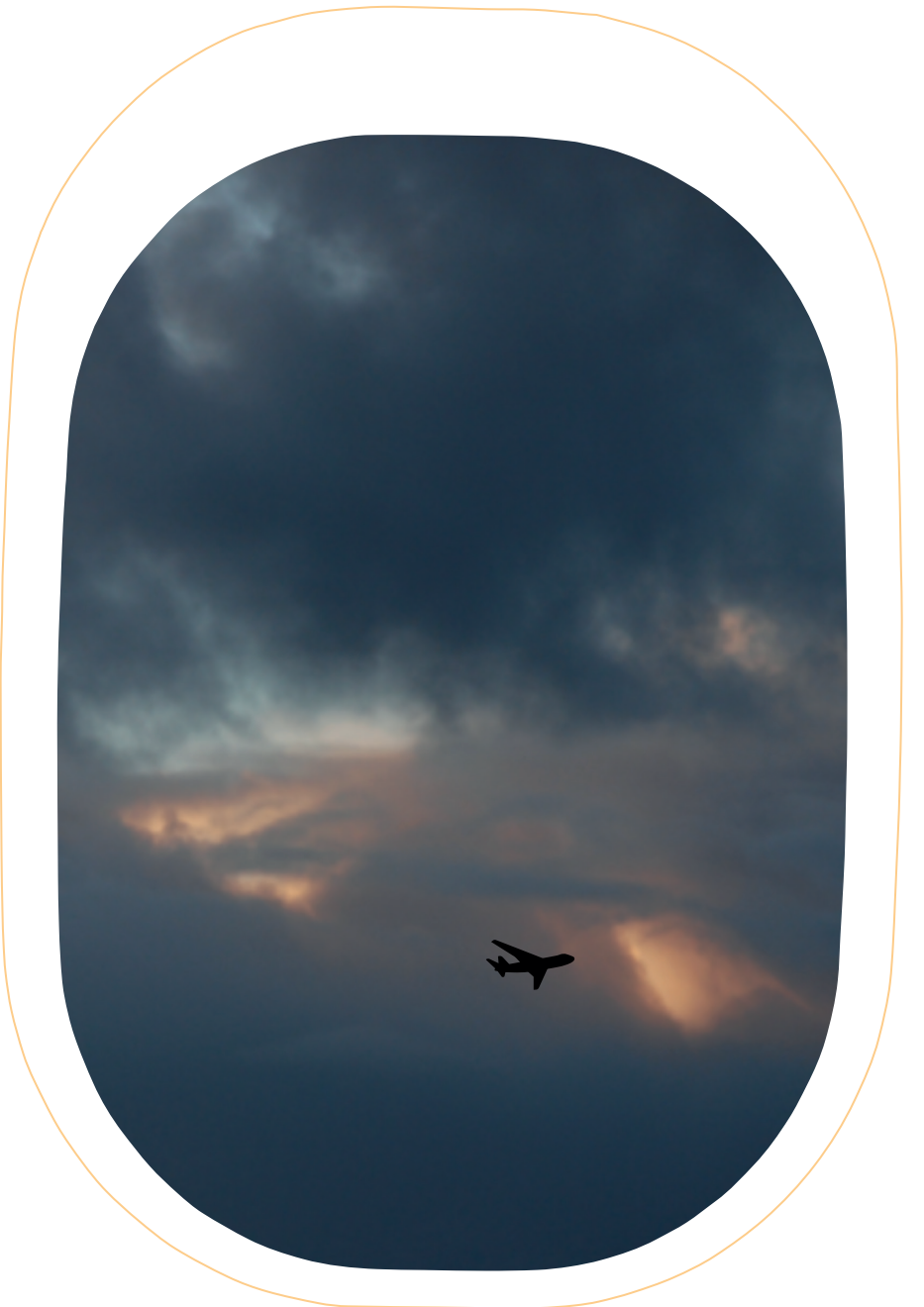

Chapter 3

Analysis of Physiological Response to Neutral Virtual Reality Worlds

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ABSTRACT

Using virtual reality technology for exposure therapy to treat patients with anxiety disorders is attracting considerable research attention. The ability to monitor patient anxiety level helps therapists to set appropriate anxiety arousing situations. Physiological measures have been put forward as objective indicators of anxiety levels. Because of individual variation, they need a baseline recording that is often conducted in neutral virtual worlds that do not include phobic stressors. Still because of the novelty of the virtual worlds, reports in the literature suggest that individuals already show some level of arousal when placed in these worlds. This paper presents two studies that look at the effect two different neutral virtual worlds can have on individuals. Findings suggest that a neutral world does not have to result in an increased level of arousal.

INTRODUCTION

Virtual Reality Exposure Therapy (VRET) is receiving considerable research attention for treatment of patients suffering from anxiety disorder, such as claustrophobia, fear of driving, acrophobia, spider phobia, social phobia, panic disorder with agoraphobia, post traumatic stress disorder, and fear of flying. VRET is based on the ideas of gradual exposure in vivo, considered the gold standard for treatment of phobias. Recent meta-studies (Gregg & Tarrier, 2007; Parsons & Rizzo, 2008; Powers & Emmelkamp, 2008) show that exposure in VR is as effective as exposure in vivo. An important element of the therapy is that the exposure is done gradually to more anxiety arousing situations. Therapists are, therefore, continuously monitoring the anxiety level of a patient. This can be done using Subjective rating of Anxiety (SUD), behavioural observations or physiological measures. The latter has the advantage of being more objective, and can be used directly by a computer to assist a therapist in a multi-patient VRET setting (Paping, Brinkman, & van der Mast, 2010). Physiological measures need however a baseline measurement because of individual variation. One often used procedure is to obtain a physiological baseline recording when the patient is placed in a neutral VR world, i.e. a VR world which should not include phobia related stressors. Even if this world has no phobia related stressor, it is not clear whether experience of being placed in a Virtual Environment (VE) causes some level of anxiety. Some authors (Wiederhold & Wiederhold, 2005) have suggested that the majority of non-phobic individuals do get some level of arousal when placed in a VE. For example Jang et al. (2002) report a study with non-phobic individuals and observed that participants were initially aroused in the VR exposure, but returned to a normal base line after approximately 7 minutes. In another study, Wiederhold et al. (1998) also report that non-phobics, when placed in a VE, initially show some level of anxiety. They argued that the VE is a new and novel stimulus and therefore causing this effect. Extending on this line of reasoning, this paper explores whether the design of the neutral world can also contribute to this effect. Or in other words, would it be possible to design a truly neutral world. As reported in this paper, we were confronted with this question after results of our first study suggested that both phobic and non-phobic participants showed higher heart rates during exposure in a neutral virtual world than both in the VE with phobic stressors and in the recovery phase after the VR exposure. Furthermore, both phobics and non-phobic individuals experienced moderate to severe nausea in the neutral VR condition. This called into question the neutrality of the neutral virtual world and led our research into the creation of neutral virtual worlds.

The paper starts with briefly discussing key concepts such as VR systems, presence and problems experienced by patients. After this, the first study is presented in which both non-phobic and phobic individuals are placed in a neutral VR world, a virtual airplane, and a recovery phase. The second study starts with a discussion of the design of a new neutral VR world. This virtual world aims to be an almost identical representation of the room the individual is sitting in. Results are presented from data collected in four conditions: the real world room, the new neutral VR world, virtual airplane, and recovery phase. The paper concludes by discussing the findings which suggests that it might be possible to design a truly neutral world. Also no support was found for a possible transfer of habitation from the physical room to the neutral virtual room.

BACKGROUND

The sense of being a part of the VE even when a person is physically situated in a totally different real world is considered a key element of VRET. This concept of presence is related to four components: technological devices; user-computer interactions; main task and the user (IJsselsteijn, de Ridder, Freeman, & Avons, 2000; Witmer, Jerome, & Singer, 2005). In the application field of VRET, the main technical devices used are a head mounted display (HMD) and a computer automatic environment (CAVE). The CAVE has a relatively higher immersion level with stereoscopic images on four to six sides around the user while the HMD has only one stereoscopic image in front of the user. In a study on the effects of VRET in patients with acrophobia using CAVE and HMD, it is reported that VRET was superior to no-treatment on anxiety, behavioural avoidance and attitudes towards heights. Although the therapy given in the CAVE resulted in higher level of presence than the therapy given through HMD, no differences in effect were found between them and the results remained stable during the following six months (Krijn, Emmelkamp, Biemond, et al., 2004). This therefore seems to suggest that only a certain level of presence is needed for treatment to be effective. Even with devices as a HMD or a CAVE patients can still experience low level of presence causing them to drop out of the treatment (Krijn, Emmelkamp, Olafsson, & Biemond, 2004). This underlines that presence is also determined by individual factors (Ling, Nefs, Brinkman, Heynderickx, & Qu, 2010) such as vision ability, cognitive processing ability (Schubert, 2009) of the VE, and personality (Wallach, 2010). It has also been suggested that imaginative power influences presence (Huang, Himle, & Alessi, 2000; Regenbrecht, Schubert, & Friedmann, 1998). Being able to visualize more vividly could intensify the experience of the VE. Cybersickness is another potential intervening factor. Cybersickness is a form of motion

sickness that occurs as a result of exposure into VE and can range from a slight headache to an emetic response (Stanney, Mourant, & Kennedy, 1998). Although physiological measurements can be used for determining anxiety during VRET, the side effect of cybersickness can also arouse physiological changes in people (Min, Chung, Min, & Sakamoto, 2004). Both cybersickness and presence therefore seem important factors that might explain, besides the initially suggested habitation, physiological effects in neutral virtual worlds.

STUDY 1

METHOD

The first study was initially set out to study physiological response of both phobic and non-phobic individuals in a VE with phobic stressors. Both groups were exposed to three conditions: a neutral virtual world, a virtual flight, and a recovery phase. Both the effects for two groups and conditions on physiological recordings and self-reported anxiety were analysed.

VR system

The VRET Delft 2007 system is described in detail elsewhere (Aslan, 2007; Brinkman, van der Mast, Sandino, Gunawan, & Emmelkamp, 2010; Gunawan, Mast, Neerincx, Emmelkamp, & Krijn, 2004; Schuemie, 2003). Briefly, the HMD used was the stereoscopic Cybermind Visette Pro with a resolution of 640x480 per display and a 60 Hz refresh rate. An Ascension Flock of Birds was used as the tracking tool. Two personal computers (PC) were used in the system, the therapist computer where the therapist controls the therapy session and a patient PC which gets input from the HMD and therapist computer. Both the neutral virtual world and the flight world were created with WorldUp R4 by Sense8.

Sound was delivered via the inbuilt HMD speakers and two additional speakers in front. Participants were seated on a normal desk chair during the neutral virtual world (Figure 1, left) and on a real passenger seat from a KLM airplane during the virtual flight (Figure 1, right). To enhance the feeling of presence in the Airplane world, two AuraSound AST-3B-4 Bass Shakers including a 100-Watt digital amplifier were added to the system.

Participants

Participants for study 1 were aviophobics that applied for therapy at the VALK foundation,

Figure 1. Left, the neutral courtyard, right, virtual flight world.

and non-paid volunteers without fear of flying who acted as a control sample. The VALK foundation is a mental health clinic that specializes in aviation related anxiety. During the recruitment period 46 phobic clients who applied for treatment received written information regarding the VR study at their home address two weeks before their first visit. Out of this group, 40 phobics were willing to participate. One client was excluded because of the use of cardioactive medication (ß-blockers). This left 39 phobic clients (15 men) with an average age of 44.5 (*SD* = 12.4), who fulfilled the DSM-IV criteria for specific situational phobia furnishing usable data. In the same period 22 non-paid volunteers without fear of flying and an average age of 48.3 (*SD* = 11.4) successfully completed a part of the same protocol. Volunteers were recruited through the social network of the research institution's staff. One of them received a positive diagnosis for aviophobia during the intake and was excluded. Another control subject's questionnaire data rendered unusable, her physiological data was included for analyses. The 21 non-phobic healthy subjects had flown at least several times; most of them had flown within 18 months of the experiment. None of the control subjects was ever treated for fear of flying. Before start of the experiment, informed consent was obtained from all participants. The research protocol has been approved by the local medical ethics committee.

Measures

For the physiological recordings, the three target variables were Heart Rate (HR), Pre Ejection Period (PEP) and Respiratory Sinus Arrhythmia (RSA). PEP is considered a measure of (activating) sympathetic cardiac control (Sherwood, et al., 1990) whereas RSA is a measure of (calming) parasympathetic control (Berntson, et al., 1994). Scoring of these variables from thorax impedance and the ECG is described in detail elsewhere (Goedhart,

Kupper, Willemsen, Boomsma, & de Geus, 2006; Goedhart, Van der Sluis, Houtveen, Willemsen, & De Geus, 2007). Briefly, from the ECG (sampling rate 1000 Hz) the HR was obtained from the time between two adjacent R waves. PEP was defined from the ECG and ICG as the time interval from the Q-wave onset, the onset of the electromechanical systole, to the B-point (from the ICG), which signals opening of the aortic valves (Sherwood, et al., 1990; Willemsen, De Geus, Klaver, Van Doornen, & Carroll, 1996). RSA was obtained from the ECG and respiration signals by subtracting the shortest IBI during HR acceleration in the inspirational phase from the longest IBI during deceleration in the expirational phase (i.e. the peak-through method)(Grossman, van Beek, & Wientjes, 1990). When no phase-related acceleration or deceleration was found, the breath was assigned a RSA score of zero. Automatic scoring of PEP and RSA was checked by visual inspection of the impedance and respiratory signal from the entire recording. Our focus on cardiac parameters reflects two major considerations: measurements needed to be as non-invasive as possible and they needed to respond to changes in psychological state over a time scale of a few minutes. The PEP and RSA measures are uniquely qualified to meet both demands (Goedhart, et al., 2006; Willemsen, et al., 1996). Using a visual display of the output of an inbuilt vertical accelerometer, we identified artefact free periods in each condition that lasted at least 5 minutes each.

All questionnaires were administered in the Dutch language, they were:

- The Subjective Units of Discomfort (SUD) scale was used to examine to what extent participants were feeling anxious at several moments. They had to indicate their perceived anxiety on a scale from 1 (“totally relaxed”) to 10 (“extremely anxious”) (Wolpe, 1973).
- The Visual Analogue Flight Anxiety Scale (VAFAS) was used to examine to what extent participants were anxious about flying. The one-tailed scale ranges from 0 (No flight anxiety) to 10 (Terrified or extreme flight anxiety) (Van Gerwen, Spinhoven, Van Dyck, & Diekstra, 1999).
- The Igroup Presence Questionnaire (IPQ) was used to measure the feeling of being in the VE. Each of the 14 items is rated on a 7-point Likert-type scale, ranging from -3 (totally disagree) to 3 (totally agree). The IPQ scale consists of 3 subscales: spatial presence, involvement and realness. The psychometric properties proved to be good to excellent (Schubert, Friedmann, & Regenbrecht, 2001). In the present study only the total score on the IPQ was used. The internal consistency in the present study was good, Cronbach’s Alpha .95

Procedure

All measurements took place at the VALK facility. Upon arrival participants were informed about the procedure. For the aviophobics it was emphasized that participating was voluntary and neither participation nor refusal to participate impacted on the quality of treatment. After informed consent was given, six electrodes were attached and connected to the Vrije Universiteit Ambulatory Monitoring System (VU AMS), which records the thorax impedance, and the ECG in freely moving individuals (Goedhart, et al., 2006; Goedhart, et al., 2007; Houtveen, Groot, & de Geus, 2006; Riese, et al., 2003; Willemsen, et al., 1996).

Participants were then seated upright in a normal chair and partook in three experimental conditions, always in the same fixed order. Participants first received a 7 minutes VR exposure in a neutral VE after which they were asked to fill out the IPQ. The neutral VE (Schuemie, 2003) consisted of a courtyard in which participants moved around under therapist control, i.e. locomotion is not controlled by the participants. The locomotion was standardized and automated. Participants completed two rounds along the outer perimeter of the courtyard (figure 1, left). This condition was followed by 7 minutes VR flight simulation in a real airplane seat. Participants were seated upright and followed a standardized program consisting of taxi-out, take-off, a short cruise flight, descent, approach and landing. Subsequently, participants were given 7 minutes of recovery time while seated in the airplane seat. Subjective units of distress (SUD) were measured at four discrete moments: before the start of the experiment, directly after both VR presentations and at the end of the recovery period. The VAFAS was administered before start of the experiment.

RESULTS

Comparison of phobic and non-phobic control participants on sociodemographic characteristics and the VAFAS scale were performed with one-way ANOVA. Table 1 shows the main characteristics for the group of phobic participants and the control group.

An ANOVA was conducted on the SUD scores collected in three conditions (neutral VR world, virtual flight, and recovery) from the two participant groups (phobic, and control). Significant condition ($F(1.73, 91.54) = 3.81$, $p = .031$) and group ($F(1, 53) = 21.68$, $p < .001$) effects were found for self-reported distress. Phobics had higher levels throughout, while on average participants reported less fear during recovery compared to the virtual

Table 1. Number of participants, gender, age, BMI and VAFAS score in study 1
BMI: Body Mass Index; VAFAS: Visual Analogue Flight Anxiety Scale.

	Phobics Mean (SD or %)	Non-phobics Mean (SD or %)
Number of participants		
• Total	39	21
• Men	15 (38%)	11 (52%)
• Women	24 (62%)	10 (48%)
Age (years)	44.5 (12.4)	48.3 (11.4)
BMI	24.6 (3.8)	23.5 (2.4)
VAFAS	8.0 (1.4)*	0.6 (0.7)

* Phobics differ from non-phobics at $p < .001$.

flight. Follow-up analyses for both groups separately showed significant differences in reported anxiety between the recovery condition and both the neutral VR world ($t(33) = 2.51$, $p = .017$) and the virtual flight ($t(33) = 3{,}09$, $p = .004$) for the flight phobics, while no significant differences between conditions were seen for the control group (Figure 2).

An ANOVA with the same independent variable was also conducted on the physiological data. Of the physiological variables, RSA had to be log (ln) transformed to obtain normal distributions. For HR a significant main effect was found for condition ($F(1.78, 101.62) = 16.94$, $p < .001$). Both control participants and phobic participants had higher heart rates during the neutral VR world than in any other condition (Figure 3). In contrast to the main effect of condition for HR, no significant effects of condition were found in RSA and PEP data. In fact, there was no significant main or interaction effect in RSA at all. A significant main group effect did emerge in PEP data, phobic participants had significantly shorter PEP values than control subjects, indicating higher cardiac sympathetic control ($F(1, 58) = 5.83$, $p = .019$).

A one-way ANOVA was conducted for the IPQ. Non-phobic subjects scored significantly higher on the total IPQ scale ($F(1, 57)=10.42$, $p=0.002$) including its subscales Spatial Presence (SP: $F(1, 57)=11.45$, $p < 0.05$) Involvement (INV: $F(1, 57)=5.24$, $p < 0.05$) and Realism (Real: $F(1, 57)=4.08$, $p < 0.05$). IPQ scores were relatively high compared with other studies.[1] No significant correlations between IPQ scores and SUD scores were found.

[1] For comparison data see www.igroup.org

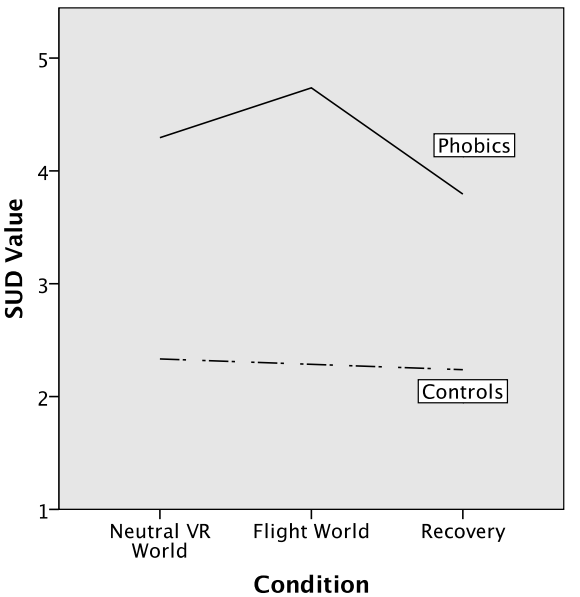

Figure 2. SUD scores for phobic and control participants. SUD: Subjective Units of Discomfort.

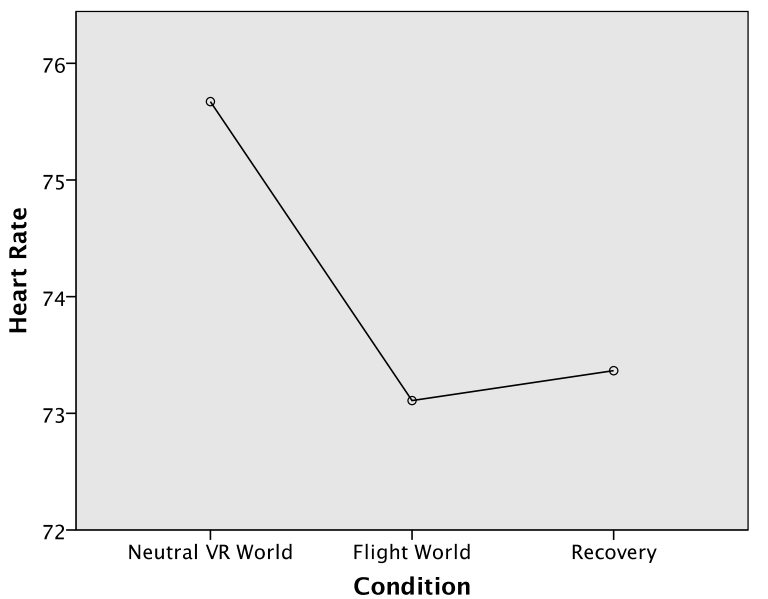

Figure 3. Average HR for phobic and non-phobic combined.

Almost all participants complained either during or directly after the neutral VE exposure about dizziness and nausea. This was corroborated by an elevated HR during this supposedly non-provocative neutral condition. No difference in anxiety between the neutral VR world and the flight world was reported by the flight phobics. All other measures did not differentiate between conditions. This led us to the conclusion that the neutral VR world probably was not truly neutral after all.

STUDY 2

METHOD

Novelty of a new environment or cybersickness might have caused the higher level of arousal in the neutral VR world in study 1. This would suggest that arousal level could be reduced by removing the novelty and therapist controlled locomotion element from the neutral VR world. The aim of the second study was therefore to examine whether a new neutral world would still result in an elevated level of arousal. In addition the study was also set out to study the suggested novelty effect or possible transfer of habituation by changing the order in which physiological recording was collected (the actual room first, or virtual room first).

VR system and new neutral world

To make a possible transfer of habitation possible a virtual world was created which was a close replication of the actual room the individual was situated in, causing participants to see the same environment when they would put on or take off the HMD. Participants were seated in front of a television (Figure 4, right) showing a documentary about wildlife. In the new neutral VR world (Figure 4, left) participants were seated in front of the same television set that showed the same documentary. Looking around with or without the HMD would give the same view of the room. The new neutral VR world ran on the same hardware as the VR flight and the old neutral VR world but used different software with exception of the Windows XP operating system. The Vizard Virtual Reality Toolkit, Vizard 3.0 was used to create an executable that provided head tracking and the image for the HMD. The model of the room was created with Autodesk Maya 2008 and textures were edited with Adobe Photoshop CS2. The model consisted of the room in which a table, television set, room dividers and a metal rail were modelled in detail. There were 18 textures made with several different sizes ranging from 2048 x 2048 pixels

(the wall closest to the patient) to 64 x 512 pixels (a table leg). The world was displayed with a resolution of 640 x 480 to match the resolution of the HMD used in VR flight. All textures where file textures. The textures were made out of photographs taken from the location where the patient would sit. Every visible face got its own unique texture. No dynamic lights or computer-generated shadows were used. Distortion was removed from the images and the colour balance of several images was altered. Some objects were edited out of textures, like the table that was removed from the photograph that formed the texture for the wall behind the television set, which was facing the patient. Shadows belonging to objects that were removed from the scene were edited out like the radio and chair in front of the table. Some shadows had to be drawn in by hand like the shadow of the table on the part of the wall behind the table. A video could be displayed on the television set triggered by a keyboard button press. The video used was ripped from DVD and recompressed with a resolution of 720 x 576 at 25 frames/second. The video format and codec used was VC-1, WMV3 (Windows) and the audio format and codec used was WMA2, 161 (Windows). The video was edited to a duration of 6 minutes and 29 seconds. A DVD with the exact same edited video was made so that the video could be played on the DVD player in the actual room.

Participants

44 People participated, 32 students who earned credits by participating and 12 non-paid volunteers recruited by means of word-to-mouth. All participants received an email with information regarding the study before start of the experiment. One participant was excluded because of the use of cardioactive medication. Another two participants were partly excluded from analyses because of equipment failure during physiological recordings; their questionnaire data was included for analysis. Average age of all 43 (16 men) participants was 25.6 (*SD* = 8.0), the youngest being 18 years old, the oldest 51.

Figure 4. Left, new neutral virtual world, right, picture of the actual room.

Measures

In addition to the three physiological measurements and questionnaires used in the previous study the following two questionnaires were added:

- The Simulator Sickness Questionnaire (SSQ) was used to examine to what extent participants experienced symptoms associated with simulator sickness caused by the VR exposure. The SSQ consists of a checklist of 27 symptoms, each of which is rated in terms of degree of severity (none, slight, moderate, severe). It is normally administered twice, before and after a VR exposure (Kennedy, & Lane, 1993). The instrument provides three subscales (Nausea, Oculomotor and Disorientation) and a composite Total Severity Score, which is used in the present study. The instrument's psychometric properties are good (Johnson, 2005). The internal consistency in the present study was good, Cronbach's Alpha .78.
- The Vividness of Visual Imagery Questionnaire (VVIQ) was used to examine the ability to form mental pictures (Marks, 1973). The vividness of the image is rated along a 5-point Likert-type scale, from 1 (perfectly clear and as vivid as normal vision) to 5 (no image at all, you only "know" that you are thinking of an object). All items for images obtained are first answered with eyes open, secondly with eyes closed. Note that a low VVI score means vivid imagery and a high score means vague imagery. The psychometric properties proved to be good to excellent (Campos & Perez-Fabello, 2009). In the present study the average score on the VVIQ was used. The internal consistency in the present study was good, Cronbach's Alpha .95.

Procedure

Participants started with filling out the VAFAS, VVIQ, and the SSQ (pre-exposure). After attachment of the electrodes of the VU AMS participants were seated upright in a normal seat. Participants randomized started either with the new neutral VR world, or the neutral real world. Participants were asked to complete the IPQ and SSQ-post-exposure directly after the neutral VR world. These two conditions were followed by 7 minutes VR flight simulation seated in a real airplane chair. Participants were seated upright and followed a standardized program consisting of taxi-out, take-off, a short cruise flight, descent, approach and landing. Subsequently, participants were given 7 minutes of recovery time while seated in the airplane seat. SUD score were recorded at five discrete moments: before the start of the experiment, directly after both neutral worlds, after the virtual flight and at the end of the recovery period. Before start of the experiment informed consent was obtained from all participants. The research protocol had been approved by the local medical ethics committee.

RESULTS

As was done with study 1, a series of ANOVAs was conducted to study the effect of two independent variables: condition (real world, new neutral VR world, virtual flight, recovery), and groups (first real world then new neutral VR world, or first new neutral VR world and then real world).

A significant main effect was found for condition ($F(2.46, 100.9) = 3.29$, $p = .032$) in the SUD scores. Participants reported lower levels of anxiety during the real world than during any other condition. Follow-up analyses for both groups separately showed a significant difference in reported anxiety between the real world and both the new neutral VR world ($t(20) = -2.32$, $p = .031$) and the virtual flight ($t(20) = -2,35$, $p = .029$) for the participants who saw the real world first (Figure 5). Interestingly no significant differences between conditions were found when the new neutral VR world was presented first.

The analysis of heart rate found a significant condition by group interaction ($F(2.19, 85.32) = 5.48$, $p = .005$), together with a main effect of condition ($F(2.19, 85.32) = 10.12$, $p < .001$). Follow-up tests revealed that HR during virtual flight was significantly lower than HR in any other condition (all $p <. 001$), while the interaction with group was driven by an increase of HR during the real world condition for the participants who saw the real world first (Figure 6).

Table 2. Number of participants, gender, age, BMI and VAFAS score in study 2
BMI: Body Mass Index; VAFAS: Visual Analogue Flight Anxiety Scale.

	Mean (SD or %)
Number of participants	
• Total	43
• Men	16 (37%)
• Women	27 (63%)
Age (years)	25.6 (8.0)
BMI	22.6 (2,8)
VAFAS	0.8 (1,2)

In contrast to the condition by group interaction for HR, no significant condition by group interactions were found for RSA and PEP. Significant main condition effects did emerge for overall RSA and PEP levels. Participants had significantly longer RSA values during virtual flight compared to all other conditions, indicating higher parasympathetic control during virtual flight ($F(3, 37) = 10.6$, $p < .001$), and significant longer PEP values during virtual flight compared to the new neutral VR world and the recovery condition ($F(3, 37) = 5.12$, $p = .003$), indicating less cardiac sympathetic control during virtual flight.

On average participants had a significant decrease in SSQ from pre- to post-presentation measurement ($t(41)=2.65$, $p=.011$). These changes from pre-to post scores on the SSQ were significantly correlated to the SUD values from the Virtual Flight such that decreased simulator sickness was accompanied by a lower anxiety score during the flight condition ($r = -.437$, $p = .003$). SSQ-post scores were significantly correlated with SUD-Flight ($r = .508$, $p = .001$) and SUD-Recovery ($r = .522$, $p < .001$). Participants with lower post presentation simulator sickness scores report lower anxiety during virtual flight and the recovery condition, while participants with higher post presentation SSQ values report more anxiety in both conditions.

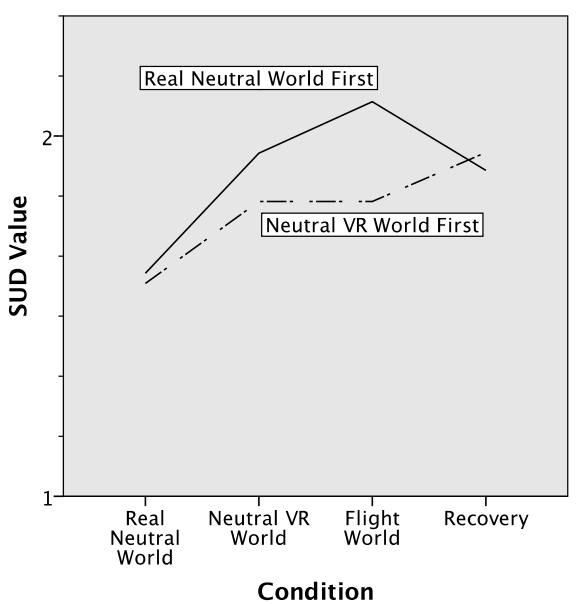

Figure 5. SUD scores for both groups. SUD: Subjective Units of Discomfort.

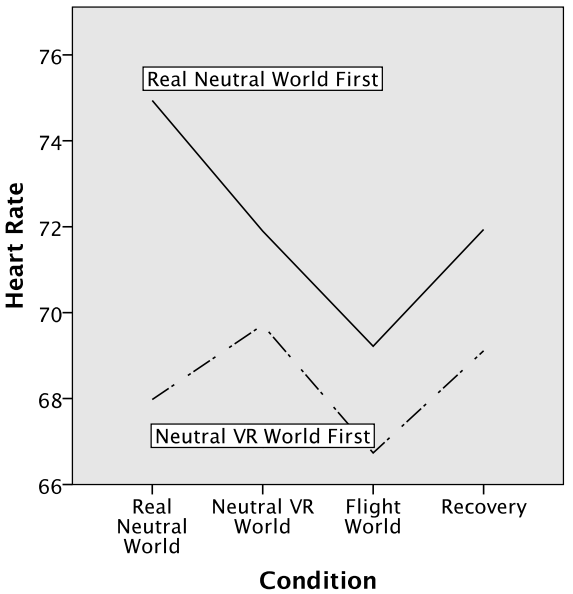

Figure 6. Average HR for both groups. HR: Heart Rate.

No significant correlations between IPQ scores, SUD scores and VVIQ were found. A significant negative correlation was found between IPQ and SSQ-Post (r = -.325, p = .033) and a significant positive correlation was found between IPQ scores and SSQ pre-post (r = .391, p = .009). On average participants with a higher presence score had a lower post-presentation simulator sickness score than participants with lower IPQ score, while participants with a higher presence score show a stronger decrease in simulator sickness compared to participants with lower IPQ scores.

CROSS COMPARISON

Cross comparison was performed on control participants from study 1 with all participants from study 2. Table 3 shows the main characteristics for both groups. ANOVAs were conducted with condition (Neutral VR world, Flight world, Recovery) and group (participants study 1, participants study 2) as independent variables. Age was added as a covariate.

Table 3. Number of participants, gender, age, BMI and VAFAS score in study 1 and 2
BMI: Body Mass Index; VAFAS: Visual Analogue Flight Anxiety Scale.

	Participants Exp.1 Mean (SD or %)	Participants Exp.2 Mean (SD or %)
Number of participants		
• Total	21	43
• Men	11 (52%)	16 (37%)
• Women	10 (48%)	27 (63%)
Age (years)	48.3 (11.4)	25.6 (8.0)*
BMI	23.5 (2.4)	22.6 (2.8)
VAFAS	0.6 (0.7)	0.8 (1.2)

* Participants study 1 differ from Participants study 2 at $p < .001$.

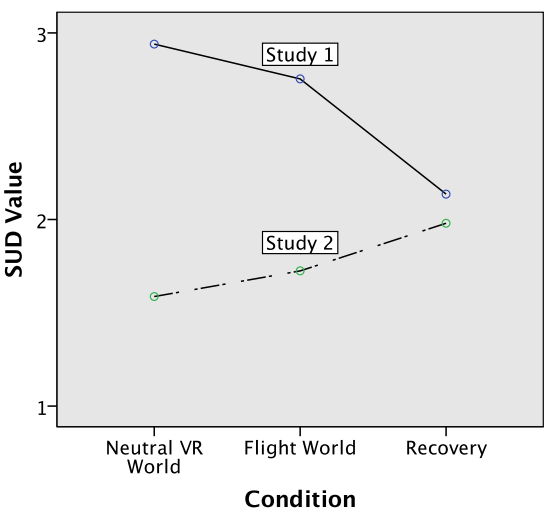

Figure 7. SUD scores for participants from both studies. SUD: Subjective Units of Discomfort.

A significant group by condition interaction was found for self-reported distress ($F(1.71, 104.1) = 6.76$, $p = .003$), together with a main effect of group ($F(1, 61) = 5.10$, $p = .028$). In figure 7 it can be seen that the control participants in study 1 had higher levels of distress throughout, while in contrast with the participants from study 2, their reported distress was highest during the neutral VR condition. In parallel with self-reported distress a significant group by condition interaction was found for heart rate $F(1.72, 101.21) = 4.57$, $p =$

.017), with a main effect for condition, not for group ($F(1.72, 101.21) = 4.21$, $p = .023$). Control participants in study 1 had significantly higher HR during the neutral VR condition than during the virtual flight and recovery condition, while participants from study 2 showed no significant difference in HR between the neutral and recovery condition.

Analogue with both subjective distress and heart rate a significant group by condition interaction ($F(2, 118) = 4.52$, $p = .013$) showed for the parasympathetic measure RSA, together with a main effect of condition ($F(2, 118) = 5.87$, $p = .004$). Post-hoc analyses revealed that participants in the second study had nearly the same RSA values during the neutral VR world and the recovery condition, while RSA values during virtual flight were significantly longer than RSA values during the neutral VR world $t(40) = 4.55$, $p < .001$ and recovery condition ($t(40) = 2.50$, $p = .016$). Differences between conditions did not reach significance for participants from the first study (Figure 8).

For the sympathetic measure PEP only a significant group by condition interaction was found ($F(1.57, 92.68) = 3.57$, $p = .042$). Again participants in the second study had no significant differences between the neutral VR world and the recovery period, with

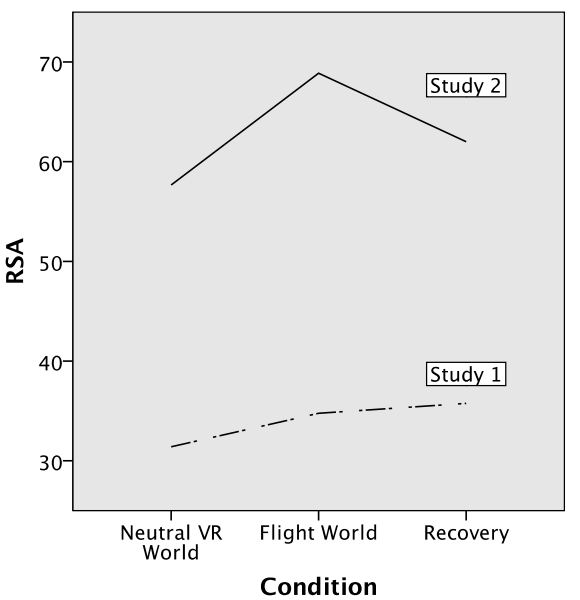

Figure 8. Average RSA for participants from both studies. RSA: Respiratory Sinus Arrhythmia.

significant longer PEP values during the virtual flight. Participants in study 1 showed no significant difference in PEP between all three conditions.

A one-way ANOVA was conducted for the IPQ. No significant differences between both groups were found.

CONCLUSION AND DISCUSSION

In the second study all physiological measures differentiated between the flight condition on one side and the VR neutral world and recovery condition on the other side, while no physiological difference was apparent between the VR neutral world and recovery. Even self-reported distress showed no significant differences between conditions when the new VR neutral world was presented first. This seems to refute the idea that a virtual world by definition will generate arousal and anxiety (Wiederhold & Wiederhold, 2005). The second study found only an interaction effect between the condition and the groups in HR. Still, follow-up analyses only found a significant decrease, instead of an increase, in HR when recordings were first collected in actual room and then in neutral VR room. This observation is therefore contra to the idea that novelty of VE would always cause arousal. Also the follow-up analyses did not find a significant difference in HR of participants from the group in which the recording took place in the opposite order (first neutral VR world, second actual room). A significant decrease would have provided support for the hypothesis of transfer of habitation from one environment to another. The lack of interaction effects in the other physiological measures makes this hypothesis again less likely. Thus suggesting that to obtain neutral physiological measurements the VE does not have to be a replication of the actual room the individual is situated in. Cross comparison of control participants of study 1 and all participants from study 2 strengthen our findings. Both subjective measures of anxiety as well as all physiological measures of arousal indicated equal anxiety and arousal in the neutral VR world and the recovery condition in the second study, while participants in study 1 had elevated values for SUD and HR during the supposedly neutral VR condition when compared to the virtual flight and recovery condition. The study also found presence and cybersickness to be negatively related. Although only a certain level of presence is needed for treatment to be effective (Krijn, et al., 2004), maximizing presence might reduce simulator sickness and thereby minimize drop out. No relationship was found between imaginative power, anxiety and presence. Our data therefore did not corroborate the idea that imaginative power influences presence (Huang, et al., 2000; Regenbrecht, et al., 1998). This might be caused

by relatively higher IPQ scores compared to other studies. It is reported that imagination has an important effect on presence when the VR is limited. However, if the VR is vivid enough, the participants do not need to use their imagination to create a convincible virtual environment (Wallach, et al., 2010). The average lower heart rate in the virtual flight condition compared to the neutral and recovery conditions could reflect different types of coping mechanisms. Our data are strongly reminiscent of similar data in dental phobics exposed to a stressful video showing surgical operations (Bosch, et al., 2001) as well as non-phobics exposed to neutral-and flight-videos (Busscher, Van Gerwen, Spinhoven & De Geus, 2010). Exposure to phobic stimuli is a complex stressor in that it can invoke both flight-flight responses, characterized by increased sympathetic and reciprocal decreased parasympathetic activity, and a passive coping response (freeze), characterized by increased sympathetic activity paired to increased parasympathetic activity. A principal finding in study 1 is that phobics were more anxious during the entire experiment than non-phobics, as expressed in significantly higher SUDs and sympathetic activation (PEP). This contributes to the validity of VR as a useful tool in exposure based therapy.

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Chapter 4

Anxiety Sensitivity moderates the relationship of changes in physiological arousal with flight anxiety during in vivo exposure therapy

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ABSTRACT

Physiological sensations and discomfort constitute the major symptoms reported by aviophobics. Anxiety sensitivity (AS) seems to moderate the relationship between self-reported somatic sensations and flight anxiety, and AS has been identified as a vulnerability factor for flight phobia. In this study we examined whether AS moderates the effects of somatic sensations and autonomic nervous system reactivity on flight anxiety induced by real flight.

In fifty aviophobics participating in Cognitive Behaviour Group Therapy (CBGT), flight anxiety, somatic sensations and autonomic nervous system reactivity were assessed during a guided return flight. Results indicate that physiological reactivity interacted with AS. Changes in heart rate and parasympathetic activity were more strongly associated with changes in reported flight anxiety for high AS participants, and less for participants low on AS. Results did not indicate a moderating effect of AS on the relationship between self-reported somatic sensations and flight anxiety.

Our results suggest that therapy for flight phobia might benefit from addressing the physical effect of anxiety, by means of cognitive restructuring and exposure to interoceptive stimuli, particularly in aviophobics high in AS.

INTRODUCTION

Taking a flight is common practice for many people in the western world, but not for all. Up to 40% of the general population in industrialized countries experience mild fear before or during flight (Curtis, 1998; Depla, Ten Have, van Balkom, & de Graaf, 2008; Van Gerwen, Diekstra, Arondeus, & Wolfger, 2004). Some 7% of all people experience serious interference in daily life and social functioning due to fear of flying (FOF). Most symptoms reported by aviophobics are related to bodily experiences (Roth, 2005; Van Gerwen, Spinhoven, Van Dyck, & Diekstra, 1999).

Fear of flying is a heterogeneous problem and can be conceptualized both as a situational phobia as well as the expression of other non-situational phobias with or without agoraphobia. Flying phobics can fear accidents, have complaints of acrophobia and claustrophobia, report panic attacks in anticipation of flights, want to be in control over the situation or are afraid to loose control over themselves. Social anxiety can be part of FOF as well (Van Gerwen, Spinhoven, Diekstra, & Van Dyck, 1997). In general, aviophobics with agoraphobia are more concerned about panic and its consequences, whereas aviophobics without agoraphobia in general report more concern about external aspects of flying like crashing (McNally & Louro, 1992).

Fear in general is often described by physical discomfort as sweating, heart racing and muscle tension. During flight one is exposed to sudden loud and strange noises, unexpected movements during turbulence, vibration, acceleration and pressure changes. All of these can lead to physical discomfort as well. While some people just notice these bodily responses, others might misinterpret these signals as danger signals. Anxiety sensitivity (AS) can be viewed as a key moderator between the experience of these bodily responses and anxiety. Anxiety sensitivity is the tendency to fear anxiety-related bodily sensations, based on the belief that the sensations have harmful consequences (Reiss, 1991). Although AS is most strongly related to panic, generalized anxiety disorder and posttraumatic stress disorder, specific phobia is also significantly associated with elevated AS (Naragon-Gainey, 2010). The meta-analysis of Naragon-Gainey indicated a correlation with a medium effect size between AS and blood/injection/injury and animal phobias, while the correlation between physical confinement (claustrophobia) and the fear of bodily harm with AS was large. Especially the physical subcomponent of the latter two showed a rather large correlation with AS.

Several studies link FOF with elevated levels of AS. Rivas and Tortella-Feliu (2000) assessed 523 non-clinical participants and found that participants with FOF had an elevated AS score, while a higher intensity of FOF was associated with a higher AS. Vanden Bogaerde and De Raedt (2008) performed a moderator analyses on questionnaire data of 160 students and concluded that AS moderates the relationship between somatic sensations and flight anxiety. Somatic sensations predicted flight anxiety in individuals with high AS, while this was not the case for students with low AS. The same authors corroborated these findings in a second more ecological valid study. Anxiety and somatic symptoms of 54 aviophobics and 49 controls without FOF were measured just before take-off on a regular line flight (Vanden Bogaerde & De Raedt, 2011). Results again showed the same moderating effect of AS on the relationship of somatic symptoms with flight anxiety. Furthermore, flight phobics had in general higher levels of AS than the control participants. While the 2008 study used a non-clinical student sample not controlled for a concurrent panic disorder, the 2011 study found similar results with a clinical sample of flight phobics without a concurrent panic disorder or anxiety disorder that was primary to the fear of flying.

Interestingly the moderating effect of AS on the relationship of bodily sensations with flight anxiety has only been studied by means of questionnaires and verbal report. Although the focus of AS lies on the experience of bodily sensations, up till now only one experimental study combined AS, FOF and actual physiological measurements (Busscher, van Gerwen, Spinhoven, & de Geus, 2010). Here measurements of AS and self-reported anxiety of 127 aviophobics were combined with measures of autonomic nervous system reactions to a neutral video and a anxiety provoking flight video. Although changes in Heart Rate (HR) and Respiratory Sinus Arrhythmia (RSA, a measure of parasympathetic activity) were correlated with changes in self-reported anxiety, AS did not moderate this association. Flight phobics who are afraid of anxiety-related bodily sensations did not report more distress than phobics who score low on this trait, even when they show stronger physiological responses. This is contra intuitive and not in line with research on AS and interoceptive awareness in other domains of anxiety related disorders. For instance, Sturges and Goetsch (1996) found that women high on anxiety sensitivity were significantly more accurate at heartbeat perception than women low on AS, although absolute heart rate did not differ across groups. Accurate perception of changes in pulse transit time and several other measures of sympathetic activity were consistently related to higher levels of AS in a study by Richards and Bertram (2000). In a review combining these and other studies by Domschke et al (2010), enhanced interoceptive awareness was characteristic of high AS individuals. The weighted mean effect size (Cohen's d) for

the relationship between AS and heartbeat perception was .63, indicating a medium to large effect. Individuals high in AS are generally more accurate perceivers of interoceptive processes associated with anxiety compared to individuals low in AS. Given the fact that high AS individuals are more accurate perceivers, that is better perceivers of anxiety related arousal, one would expect higher levels of self-reported anxiety in these high AS individuals when arousal is indeed elevated in anxiety provoking situations.

The aim of this study was to investigate to what extent flight phobics who score high on AS and who react with an increase in physiological arousal to phobic stimuli report a higher flight anxiety than aviophobics who score low on AS, even when these individuals show a concordant increase in physiological arousal. First, we tried to replicate the findings of our colleagues (Vanden Bogaerde & De Raedt, 2011) regarding the moderating effect of AS on self-reported somatic sensations and flight anxiety. Next, we tried to extend their findings by including measurements of autonomic nervous system reactions induced by real flight into our analyses.

METHOD

Participants

The 50 participants in this study were aviophobics who participated in a treatment program for fear of flying at the VALK foundation in Leiden, The Netherlands. The VALK Foundation is a collaborative venture by the Leiden University, Amsterdam Airport Schiphol, KLM, Transavia.com, Martinair and ArkeFly, specialized in treating fear of flying (FOF). The treatment program starts with a diagnostic assessment during the first visit in Leiden, followed by individual therapeutic sessions and a two day cognitive-behavioral group treatment (CBGT) as described in detail elsewhere (Van Gerwen, Spinhoven, & Van Dyck, 2006; Van Gerwen, Spinhoven, Diekstra, & Van Dyck, 2002). Most participants were self-referrals, some were referred by health care agencies, health professionals and company health programs. Airline personnel were excluded from this study. Other reasons for exclusion were current use of cardioactive medication like β blockers and a concurrent panic disorder of such severity according to the treating clinician that it would seriously interfere with the treatment of fear of flying. 79 individuals with aviophobia were considered eligible and participated in this study. Inclusion criteria for this study were complete data on all essential questionnaires (ASI, SUD, VAFAS) and complete data of all physiological variables (HR, RSA, PEP) during both flights. The security check at the airport appeared to be a major barrier for the physiological measurements.

The ambulatory measurement device and attached electrodes required a physical padding of all participants. After security screening 19% of the recording devices did not record all variables properly. Physiological data of two participants was lost due to equipment failure. One flight was cancelled due to adverse weather, excluding another 2 participants. Finally, ten participants were excluded from analyses because of incomplete data on the relevant questionnaires. This left 50 phobic clients (22 men) with an average age of 38,4 (S.D. = 10,6). Extensive missing value analysis on all physiological data and all questionnaire data available revealed no systematic differences between the fifty remaining participants and the 29 participants with incomplete data, with only small effect sizes for differences between both groups on questionnaire data ($\eta^2 < .01$). The largest effect size on the physiological variables was found for differences in HR during taxi-out on the first flight: $\eta^2 = .014$.

INSTRUMENTS

Physiological recordings

Heart Rate (HR), Respiratory Sinus Arrhythmia (RSA) and the Pre-Ejection Period (PEP) were recorded using the VU-AMS (version 4.6, Vrije Universiteit Amsterdam, The Netherlands; www.vu-ams.nl). The VU-AMS is a light-weight ambulatory device that records the impedance cardiogram (ICG) and electrocardiogram (ECG) continuously in freely moving subjects by means of six Ag-AgCl electrodes attached to the torso region (De Geus, Willemsen, Klaver, & van Doornen, 1995; Willemsen,G.M.H., De Geus, Klaver, Van Doornen, & Carrol, 1996). The apparatus has an inbuilt vertical accelerometer, which output can be used to select movement free periods for analysis. The RSA is a measure of parasympathetic control (Berntson et al., 1994), whereas PEP is considered a measure of sympathetic cardiac control (Sherwood et al., 1990). HR can be viewed as the resultant of both control mechanisms. In general, stimulation of the parasympathetic system will decrease the heart rate, while stimulation of the sympathetic system will increase the heart rate and the force of contraction. Scoring of these variables was automatic, followed by visual inspection of the impedance and respiratory signal from the entire recording. Details on scoring of these variables, recording methodology, reliability and validity are describes elsewhere (De Geus et al., 1995; Goedhart, Kupper, Willemsen, Boomsma, & de Geus, 2006; Goedhart, van der Sluis, Houtveen, Willemsen, & de Geus, 2007; Houtveen, Groot, & de Geus, 2006; Riese, 2003; Willemsen,G.M.H. et al., 1996). Briefly, from the ECG (sampling rate 1000 Hz) the HR was obtained from the time between two adjacent R waves. PEP was defined from the ECG and ICG as the time interval from

the Q-wave onset, the onset of the electromechanical systole, to the B-point (from the ICG), which signals opening of the aortic valves (Sherwood et al., 1990; Willemsen,G.M.H. et al., 1996). RSA was obtained from the ECG and thorax impedance derived respiration signals by subtracting the shortest IBI during HR acceleration in the inspirational phase from the longest IBI during deceleration in the expirational phase (i.e. the peak-through method) (Grossman, van Beek, & Wientjes, 1990). When no phase-related acceleration or deceleration was found, the breath was assigned a RSA score of zero. Our focus on cardiac parameters reflects three major considerations: measurements needed to be as non-invasive as possible, they needed to respond to changes in psychological state over a time scale of a few minutes and they needed to be reliable in an ambulatory setting. The HR, PEP and RSA measures are uniquely qualified to meet these demands (Goedhart et al., 2006; Willemsen,G.M.H. et al., 1996).

QUESTIONNAIRES

All questionnaires were administered in the Dutch language.

Visual Analogue Flight Anxiety Scale (VAFAS)
The one-tailed visual analogue flight anxiety scale was used at initial diagnostic assessment and after the second flight to examine to what extent participants were anxious about flying. The scale ranges from 0 ("no flight anxiety") to 10 ("terrified or extreme flight anxiety") (Nousi, Van Gerwen, & Spinhoven, 2008a).

Flight Anxiety Situations (FAS) questionnaire
This 32-item self-report inventory administered at initial assessment and after the second flight assesses anxiety related to flying experienced in different flight or flight related situations on a five point Likert scale. The questionnaire consists of three subscales: (a) an Anticipatory Flight Anxiety Scale, containing 14 items that pertain to anxiety experienced when anticipating a flight, (b) an In-Flight Anxiety Scale, containing 11 items measuring anxiety experienced during a flight and (c) a Generalized Flight Anxiety Scale, containing seven items assessing anxiety experienced in connection with airplanes in general (Nousi et al., 2008a; Van Gerwen et al., 1999). The internal consistency of the subscales of the FAS in the present study was good to excellent, Cronbach's Alpha ranging from .86 to .95.

Flight Anxiety Modality (FAM) questionnaire
The FAM is a 23 item self-report inventory that was used to assess the symptoms by

which flying related anxiety was expressed at initial assessment and after the second flight. Each symptom is rated on a 5-point Likert-type scale. The questionnaire consists of two subscales: (a) a Somatic Modality scale, pertaining to physical symptoms and (b) a Cognitive Modality scale, related to the presence of distressing cognitions (Nousi et al., 2008a; Van Gerwen et al., 1999). The internal consistency of the two subscales of the FAM in the present study was good at the initial diagnostic assessment phase, Cronbach's Alpha respectively .85 and .90, and acceptable to excellent after the second flight, Cronbach's Alpha respectively .76 and .94.

Anxiety Sensitivity Index (ASI)

The Dutch version of the Anxiety Sensitivity Index (Reiss, 1986; Vancleef, 2006) was administered once during the initial diagnostic assessment to assess the degree to which participants are concerned about possible negative consequences of anxiety related sensations. The 16 self-report items are rated on a 5-point Likert-type scale. For the operationalization of anxiety sensitivity (AS) we used the total score on the ASI. Cronbach's Alpha in the present study was .83.

Subjective Units of Discomfort (SUD)

The Subjective Units of Discomfort scale was verbally administered to each participant individually during taxi-out flight 1 to examine to what extent participants were feeling anxious. The one-tailed scale ranges from 1 ("totally relaxed") to 10 ("extremely anxious") (Wolpe, 1973).

Procedures

Anxiety sensitivity, flight phobia (FAS, FAM and VAFAS) and related psychopathology were assessed during the initial diagnostic assessment by questionnaires on fears and phobias in general and fear of flying in particular, followed by a semi-structured interview by a fully qualified clinical psychologist. Written informed consent was obtained from all participants at this stage as well. The local medical ethics committee approved the research protocol. At the end of this assessment phase the therapist proposed a treatment plan based on individual needs. The ensuing individualized preparation phase consisted of one to four therapeutic sessions covering relaxation and breathing techniques, psychological factors involved in fear and anxiety, and coping skills. Acrophobia, claustrophobia, traumatic social events and traumatic transportation accidents were addressed if applicable.

All participants started CBGT five weeks after initial assessment. Upon arrival for the second day of CBGT six electrodes were attached and connected to the ambulatory monitoring device. The second day of CBGT is focused on exposure, with at the end a guided return flight within Europe. Both flights were regular commercial flights with a flying time of around one hour. On average a CBGT group consisted of eight patients, a fully qualified psychotherapist and a pilot. The experimental data collection focussed on these two flights.

During taxi-out of the first flight a SUD was verbally administered to each participant individually. Using a visual display of the output of an inbuilt vertical accelerometer of the ambulatory monitoring device in combination with a log kept by the therapist and accompanying pilot we identified artefact-free periods that lasted 5 minutes each during taxi-out flight 1 and taxi-in flight 2. After disembarkation, some thirty minutes after taxi-in of flight 2 participants filled out questionnaires on flight phobia (FAM, FAS and VAFAS). Thereafter, the electrodes and the ambulatory recording device were removed.

Data analysis

The first aim of this study was to replicate the findings of Vanden Bogaerde and De Raedt (2011) regarding the moderating effect of AS on self-reported somatic sensations and flight anxiety. The SUD score during taxi-out of the first flight was used as dependent variable, analogue to the Visual Analogue Scale (VAS) measurement used by Vanden Bogaerde and de Raedt. In addition, we repeated the analysis with the VAFAS scores after the second flight as an alternative dependent variable. Anxiety sensitivity (AS) and the somatic modality subscale (FAM-after flight) were used as independent variables. The product of the FAM somatic modality subscale scores with the AS scores was added to the regression models to test for an interaction between somatic sensations and anxiety sensitivity.

The second aim of this study was to extend the findings of Vanden Bogaerde and De Raedt (2011) by including measurements of autonomic nervous system reactions induced by real flight into the analyses. In order to do so we created change scores for each of the three autonomic variables (HR, RSA and PEP) that reflected the reactivity to both flights. Change scores were defined as the value during taxi-in of the second flight minus the value during taxi-out of the first flight. Flight anxiety after the second flight (VAFAS) was again used as dependent variable. In addition we also assessed the flight anxiety change scores (VAFAS after exposure minus VAFAS at diagnostic assessment). Negative change scores reflect higher reactivity for HR, and lower reactivity for RSA and PEP. Physiological

change scores, AS scores and the product of the physiological change scores with the AS scores were used as independent variables in multiple regression, to test the hypotheses that AS moderates the relationship of physiological reactivity with flight anxiety and change in flight anxiety.

All independent variables were standardized to eliminate multicollinearity problems and to be able to report the correct regression coefficient B (Aiken & West, 1991). RSA was first log (ln) transformed to obtain normal distributions.

RESULTS

Clinical characteristics

As shown in table 1, scores on the VAFAS and all FAM en FAS (sub-) scales at the assessment phase were in line with the established norms for these questionnaires (Nousi et al., 2008a). Post flight scores were slightly above post treatment scores reported by Nousi et al. (2008b) for 251 participants who underwent the same therapy previously. Differences between scores can be explained by time of measurement, as Nousi et al. collected data three months after treatment, while our participants filled out questionnaires 30 minutes after the second flight. Anxiety sensitivity scores were slightly above scores reported for 160 participants with specific phobia by Naragon-Gainey (2010) in a meta-analyses on AS and anxiety disorders, but very much in line with scores reported by Vanden Bogaerde and De Raedt (2011) with 54 flight phobics. Table 2 shows pre- and post-exposure physiological variables. Eta square (η^2), being the effect size statistic for repeated measures ANOVA, showed a large effect for all measures. By convention, η^2 values of .01, .06, and .14 are interpreted as small-, medium-, and large effect sizes, respectively.

Regression Analyses

We started with multiple regression analyses without physiological variables in an effort to replicate the findings of Vanden Bogaerde and De Raedt (2011). We were unable to reproduce their outcome. Results indicated no interaction effects and no main effect for AS and somatic sensations on the SUD score during taxi-out of the first flight. Only with flight anxiety (VAFAS) after flight instead of the SUD as dependent variable a main effect for somatic sensations showed up $t(46) = 2.77$, $p = .008$), but still no effect for AS nor an interaction effect was seen (table 3).

Table 1. Measures of flight-related anxiety and somatic complaints at pre- and post-treatment.

	Assessment score		After second flight		
	Mean	SD	Mean	SD	Effect size (η^2)
FAS					
Anticipatory anxiety	43.0	8.5	25.8*	15.5	.510
In-flight anxiety	37.4	8.4	19.5*	7.0	.807
Generalized flight anxiety	13.2	4.9	8.9*	2.3	.444
Sum score	104.1	18.1	60.0*	21.6	.748
FAM					
Somatic complaints	26.6	9.2	15.9*	4.0	.647
Cognitive complaints	23.9	7.8	11.7*	5.3	.732
AS	33.1	9.4	-	-	
VAFAS	7.9	1.3	2.1*	1.7	.904

* Assessment score differ from post-flight score at *P < .001
FAS = Flight Anxiety Situations Questionnaire, FAM = Flight Anxiety Modality Questionnaire, VAFAS = Visual Analogue Flight Anxiety, AS = Anxiety Sensitivity, as measured by the Anxiety Sensitivity Index (ASI) questionnaire.

Table 2. Mean and S.D. of the three physiological variables HR, RSA and PEP before and after the exposure flights.

	Taxi-out 1		Taxi-in 2		
	Mean	SD	Mean	SD	Effect size (η^2)
HR	97.7	15.0	84.6**	12.4	.719
RSA	28.3	18.7	33.4*	21.1	.154
PEP	87.3	15.0	91.8*	16.8	.204

* Pre-flight (Taxi-out 1) score differ from post-flight (Taxi-in 2) score at * P < .005 and ** P < .001
HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

Table 3. Regression analyses of flight anxiety (VAFAS) on Anxiety Sensitivity (AS), Somatic Sensations (FAM) and their interaction.

	B	*SE*	*t*	*p*	Zero-order correlation
Step 1					
Constant	2.080	.217	9.582	<.001	-
AS-assessment	.076	.233	.325	.747	.182
FAM-after exposure	.655	.233	2.804	.007	.412
Step 2					
Constant	2.077	.229	9.086	<.001	-
AS-assessment	.070	.270	.260	.796	.182
FAM-after exposure	.655	.236	2.774	.008	.412
Interaction AS-FAM	.008	191	.042	.967	.085

VAFAS = Visual Analogue Flight Anxiety, FAM = Flight Anxiety Modality Questionnaire (somatic subscale), AS = Anxiety Sensitivity, as measured by the Anxiety Sensitivity Index (ASI) questionnaire.

Next, the hypothesis was tested that phobics who score high on anxiety sensitivity in combination with a heightened physiological arousal to flight exposure show a higher flight anxiety than aviophobics who score low on AS, even when these individuals show a concordant elevated physiological arousal. Physiological reactivity to flight predicted flight anxiety after the flight ($F(7, 42) = 3.00$, $p = .012$, R-Square = .333) and pre- to post flight changes in flight anxiety ($F(7, 42) = 7.46$, $p < .001$, R-Square = .554). A main effect for physiological reactivity emerged for both anxiety variables. Higher HR reactivity to flight was associated with less flight anxiety after exposure and a stronger decrease in flight anxiety over both flights. In addition, lower RSA reactivity was associated with less flight anxiety after exposure and a stronger decrease in flight anxiety over both flights (tables 4 and 5)[1].

[1] Analyses over both flights separately produced similar results.

Table 4. Regression analyses of flight anxiety (VAFAS) on Anxiety Sensitivity (AS), physiological measures (HR, RSA and PEP) and their interaction.

	VAFAS After exposure				
	B	*SE*	*t*	*p*	Zero-order correlations
Step 1					
Constant	2.080	.211	9.880	<.001	-
AS-assessment	.341	.226	1.507	.139	.182
HR Reactivity	.846	.273	3.097	.003	.410
RSA Reactivity	.433	.233	1.859	.070	.040
PEP Reactivity	.025	.266	.096	.924	-.268
Step 2					
Constant	2.193	.266	9.718	<.001	-
AS-assessment	.590	.256	2.305	.026	.182
HR Reactivity	1.000	.312	3.204	.003	.410
RSA Reactivity	.562	.248	2.272	.028	.040
PEP Reactivity	.305	.350	.872	.388	-.268
Interaction AS-HR	-.013	.292	-.045	.964	-.009
Interaction AS-RSA	.589	.287	2.051	.047	.193
Interaction AS-PEP	.110	.313	.352	.726	-.059

VAFAS = Visual Analogue Flight Anxiety, AS = Anxiety Sensitivity, as measured by the Anxiety Sensitivity Index (ASI) questionnaire, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

Post-hoc simple slope analyses revealed that in the group of high AS participants changes in HR significantly predicted changes in flight anxiety (B = .761, $t(46)$ = 2.00, p = .05), in such a way that decreased fear was accompanied by the highest HR reactivity. This relationship was not significant for the group of low AS participants (B = .211, $t(46)$ = .510, p = .612) (fig 1 left panel). For the group of high AS participants, changes in RSA did significantly predict changes in flight anxiety (B = 1.38, $t(46)$ = 3.15, p = .003) whereas this relationship was not significant for participants in the low AS group (B = -.186, $t(46)$ = -.507, p = .614) (fig 1 right panel).

Table 5. Regression analyses of changes in flight anxiety (VAFAS) on Anxiety Sensitivity (AS), physiological measures (HR, RSA and PEP) and their interaction.

	VAFAS Reactivity				
	B	*SE*	*t*	*p*	Zero-order correlation
Step 1					
Constant	-6.021	.194	-31.08	<.001	-
AS-assessment	.515	.208	2.471	.017	.263
HR Reactivity	.803	.251	3.197	.003	.320
RSA Reactivity	.867	.214	4.043	<.001	.279
PEP Reactivity	-.091	.245	-.370	.713	-.298
Step 2					
Constant	-5.829	.188	-31.01	<.001	-
AS-assessment	.861	.213	4.037	<.001	.263
HR Reactivity	1.046	.260	4.021	<.001	.320
RSA Reactivity	1.030	.206	4.993	<.001	.279
PEP Reactivity	.424	.291	1.457	.153	-.298
Interaction AS-HR	.500	.243	2.054	.046	.211
Interaction AS-RSA	.895	.239	3.743	.001	.204
Interaction AS-PEP	.305	.261	1.169	.249	-.128

VAFAS = Visual Analogue Flight Anxiety, AS = Anxiety Sensitivity, as measured by the Anxiety Sensitivity Index (ASI) questionnaire, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

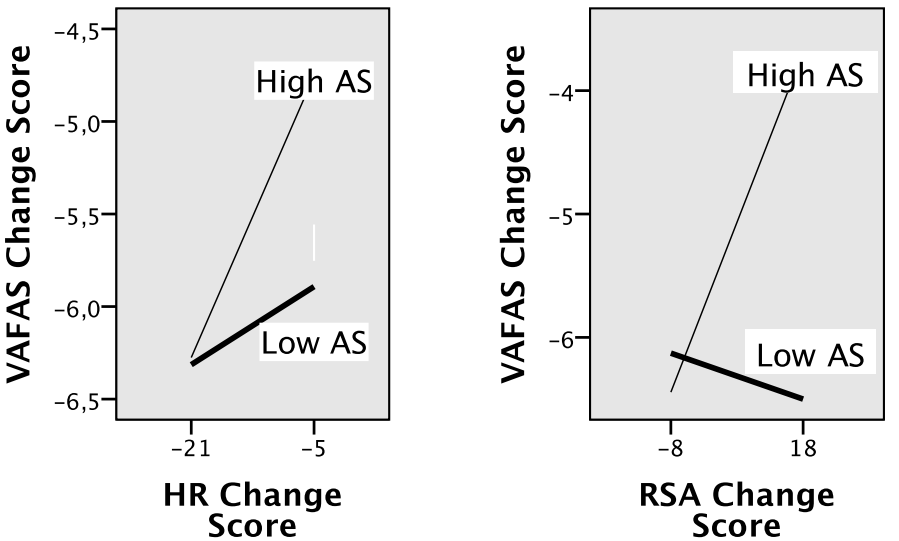

Figure 1. Simple slope regression lines for HR change scores, RSA change scores and flight anxiety change scores (VAFAS), for low AS and high AS aviophobics. A negative VAFAS change score implies decreased flight anxiety from pre- to post-measurement. A negative HR change score implies higher HR reactivity to flight, and a positive RSA change score implies a higher parasympathetic reactivity. FAM = Flight Anxiety Modality Questionnaire. VAFAS = Visual Analogue Flight Anxiety Scale. HR = Heart Rate. RSA = Respiratory Sinus Arrhythmia.

DISCUSSION

This study explored the relationship between anxiety sensitivity, somatic sensations, physiological arousal and fear of flying. In fifty aviophobics participating in CBT to overcome fear of flying, cardiac autonomic responses were assessed during two guided exposure flights. Results indicate that physiological reactivity predicted flight anxiety after the exposure as well as changes in reported flight anxiety. Furthermore, physiological reactivity interacted with anxiety sensitivity. Changes in heart rate and parasympathetic activity were more strongly associated with changes in reported flight anxiety for high AS participants, and less for participants low on anxiety sensitivity.

Flight phobia has been linked to elevated levels of anxiety sensitivity (Naragon-Gainey, 2010; Vanden Bogaerde & De Raedt, 2008; Vanden Bogaerde & De Raedt, 2011). In our sample of aviophobics, AS scores were very much in line with these findings as well as with AS scores previously found for participants with specific phobia (Rivas & Tortella-Feliu, 2000). According to Clark's cognitive approach to panic (Clark, 1986), normal autonomic anxiety responses are catastrophically misinterpreted as much more dangerous than they really are. This misinterpretation leads to increased fear and anxiety, which leads to even more bodily sensations, creating a vicious cycle. Anxiety sensitivity is thought to be the moderating key element in this relationship between somatic sensations and anxiety, the driving force between awareness of the aversive bodily sensations and the misinterpretation as danger signals (Reiss, 1991). Up till now only questionnaires and verbal report have been used to assess this relationship with aviophobics. This study is the first to include actual physiological arousal.

Our results indicate that the addition of physiological markers of arousal strengthens the model of cognitive misinterpretation of bodily sensations, in such a way that a higher HR reactivity was associated with a stronger reduction in flight anxiety for all participants, but more so for aviophobics who score high on AS. Individuals high in AS are known to be better perceivers of heartbeat activity than persons low on AS (Domschke et al., 2010). In view of our results it seems that changes in heartbeat influences anxiety in participants who are susceptible to interpret normal bodily sensations in a threatening manner. Interestingly, low parasympathetic reactivity to flight further contributed to a decrease in flight anxiety after exposure. Increased parasympathetic activity when exposed to frightening stimuli was seen in some dental phobics and blood phobics, and resembles a passive coping response, characterized by increased sympathetic activity paired to a concurrent increase in parasympathetic activity (Bosch et al., 2001; Bosch, de Geus,

Veerman, Hoogstraten, & Nieuw Amerongen, 2003; Sarlo, Palomba, Angrilli, & Stegagno, 2002). High AS has been associated with accurate perception of several measures of sympathetic activity (Richards & Bertram, 2000), but to our knowledge there is no research linking parasympathetic (RSA) changes to interoceptive awareness. Our results indicate that a sympathetically driven HR reactivity paired to low parasympathetic reactivity to actual flight was associated with decreased flight anxiety. The lack of interaction between AS, FOF and actual physiological reactivity to phobic video stimuli previously reported by the same authors (Busscher et al., 2010) might have been caused by the low ecological validity of the used stimuli. The current study used in vivo exposure during two actual flights.

We were unable to reproduce the moderating effect of AS on the relationship between self-reported somatic sensations and flight anxiety as reported by Vanden Bogaerde and De Raedt (2008, 2011). In their most recent study they asked flight phobics and control participants just before take-off, while already seated in the airplane, to indicate how anxious they were using a Visual Analogue Scale (VAS), and their bodily sensations using the FAM somatic subscale. The VAS normally measures state anxiety (Davey, Barratt, Butow, & Deeks, 2007) and not flight anxiety. To replicate their analyses we used the SUD value during taxi-out of the first flight, which is comparable to their VAS. We also performed the regression analyses with the VAFAS, a true measure of flight anxiety. Although a positive correlation existed between somatic sensations and flight anxiety, no moderating effect of anxiety sensitivity emerged on the relationship of somatic sensations with either the SUD or VAFAS. It seems that flight phobics who are afraid of anxiety-related bodily sensations do not report more flight anxiety or distress than phobics who score low on this trait, even when they report more somatic sensations. Vanden Bogaerde and De Raedt (2011) used the combined sample of aviophobics (n = 54) and controls (n = 49) in their moderator analyses. We performed our study only in aviophobics seeking treatment. The difference in results might be partly due to the inclusion of control participants in their analyses.

Although AS generally is seen as a stable dispositional variable, cognitive behavioural therapy (CBT) is efficacious in reducing AS. In a meta-analytic review large effect sizes for CBT in reducing AS in clinical and at risk samples are reported (Smits, Berry, Tart, & Powers, 2008). Likewise, a meta-analytic review on AS and anxiety disorders shows that changes in AS correspond with changes in anxiety symptoms (Olatunji & Wolitzky-Taylor, 2009). In their review on interoceptive sensitivity Domschke et al (2010) remark that regardless of the accuracy of the interoceptive perception, individuals high in AS show heightened

reactivity to these sensations. Moreover, they conclude that behavioural and cognitive interventions, especially cognitive restructuring, exposure to interoceptive stimuli and biofeedback using heart rate, are effective in modifying a putative stable trait as AS.

We did not measure perception of arousal during the flight, nor did we measure cognitive misinterpretation in real-time. Consequently, we have to be prudent with therapeutically recommendations. However, it seems reasonable to assume that, although not measured, participants most probably were able to perceive their (increased) heartbeat. As changes in heartbeat were associated with anxiety reduction, more focused exposure to these physiological symptoms might be a clinical implication of the present findings. The fact that this association was more pronounced in participants high on AS can be interpreted in various ways, because neither perception nor interpretation of physical symptoms has been assessed in real time in the present study. However, persons with elevated levels of AS are known to habitually attend to bodily sensations and to interpret normal autonomic anxiety responses as much more dangerous than they really are. Possibly, cognitive interventions in addition to exposure to bodily sensations might be particularly useful in those participants who are more likely to attend to these sensations and to interpret them catastrophically (Oakes & Bor, 2010; Wells & Papageorgiou, 2001; Wild, Clark, Ehlers, & McManus, 2008). Evidently, future research assessing perception and interpretation of bodily sensations in participants varying in anxiety sensitivity during actual flight seems warranted.

The strength of the current study is the use of a relatively large sample of true aviophobics seeking treatment, in combination with in vivo exposure and actual psycho-physiological measurements. To our knowledge only a few studies used comparable numbers of true aviophobic participants in real live exposure but without including psychophysiological measurements [e.g., Van Gerwen et al (2003, 2006), Howard et al (1983)]. Burger (2011) took ECG recordings from 24 aviophobic individuals during a fear of flying seminar including exposure in a simulator and two actual flights. Many other studies on fear of flying used limited number of participants [(Holmes et al (1979) n=5; Haug et al (1987) n=10; Ekeberg et al (1989, 1990, 1990) n between 13 and 34; Wilhelm and Roth (1997a, 1998b, 1998a) in a series of publications based on the same experiment n=28 women], lacked in-vivo exposure [Busscher et al (2010); McNally and Louro (1992); Wilhelm and Roth (1997b); Bornas et al (2006a, 2006b, 2007)], made use of non-clinical participants (Vanden Bogaerde & De Raedt, 2008), or used a combination of low numbers, students and no in vivo exposure [Bornas et al (2004, 2005) n=15].

This study also has several shortcomings. Aviophobics generally score high on AS, and did so in this experiment. This limits the range of scores and hence predictive power. The anxiety sensitivity questionnaire was administered only once, at the very first beginning of the therapy, while the FAM, FAS and VAFAS were taken at the beginning and once more at the end. Although AS is regarded as a relatively stable trait, as mentioned before CBT is known to be efficacious in reducing AS. The individual therapeutic sessions and CBGT were not specifically aimed at reducing AS, nevertheless AS might have been reduced as a side effect in the course of the experiment. Another limitation is the high study drop-out due to equipment failure, the security screening before the flights and incomplete questionnaire data. Extensive missing data analyses however showed no systematic differences between completers and the lost participants. Moreover, the VAFAS was only administered at initial diagnostic assessment and after the second flight and consequently change scores on the VAFAS may also reflect the effect of the individual preparation phase and the first day of group treatment preceding the exposure flights. Also, the semi-structured interview used during assessment was not validated to verify diagnosis of simple phobia. A further limitation of the current study, which precludes conclusions about cause and effect relationships, lies in the correlational design. Longitudinal and controlled trials could further clarify the relationship of AS, somatic sensations, physiological reactivity and fear of flying.

In conclusion, we found a positive correlation between somatic sensations and flight anxiety, but no proof that AS moderates this relationship. The addition of physiological markers of anxiety, especially HR, strengthens the model of cognitive misinterpretation of bodily sensations. A stronger reactivity in HR was associated with a stronger reduction in flight anxiety for all aviophobics, but more so for participants high on AS. Results indicate that CBT for FOF might benefit from addressing somatic sensations and the physical effect of anxiety, by means of cognitive restructuring and exposure to interoceptive stimuli, particularly in aviophobics high in AS.

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4

Chapter 5

Cognitive coping as a mechanism of change in cognitive-behavioural therapy for fear of flying; a longitudinal study with 3-year follow-up

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ABSTRACT

Objectives: To examine the predictive value of cognitive coping strategies at pre-treatment and the value of changes in these strategies during cognitive-behavioral treatment for aviophobia for long-term therapy results.

Method: Data from baseline, after therapy at 2 months, short-term follow-up at 5 months and long-term follow-up at 41 months were analyzed (N = 59).

Results: Participants were in a long-term process of change, which continued positively after therapy for maladaptive cognitive coping strategies. The use of cognitive coping strategies at baseline was not predictive of long-term outcome. However, a greater increase in the use of adaptive coping strategies, and more importantly, a greater decrease in the use of maladaptive coping strategies were predictive of improvements indicated in self-report of flight anxiety and actual flight behavior at long-term follow-up.

Conclusion: Improvement of maladaptive cognitive coping strategies is possibly a key mechanism of change in cognitive-behavioral therapy for aviophobia.

INTRODUCTION

Individual differences in emotion regulation are associated with well-being, successful functioning and mental health (Aldao et al. 2010; Berking and Wupperman 2012; Rooij et al. 2014). The broad concept of emotion regulation refers to the conscious and unconscious physiological, behavioral and cognitive processes that modulate emotions to respond appropriately to environmental demands (Thompson 1994). Within emotion regulation, cognitive coping can be seen as a conscious strategy to deal with (primarily) negative events and stressful situations, and the thoughts related to these situations. Some cognitive coping strategies seem more adaptive than others, while the use of certain maladaptive cognitive coping strategies has been linked to psychopathology (Aldao et al. 2010; Rooij et al. 2014; Potthoff et al. 2016). Strikingly, almost no studies of anxiety problems have been done as to whether psychological interventions may change the use of specific coping strategies, and if so, whether these changes predict subsequent reductions in anxiety. The present study examined whether coping strategies at pre-treatment and changes in coping strategies during cognitive-behavioral treatment are predictive of fear of flying at 3-year follow-up in a group of aviophobic patients.

Coping styles and anxiety

Numerous studies have examined the relationship of different coping styles with anxiety. The preferential and predominant use of cognitive coping strategies can be split into two separate styles: an adaptive style inversely associated with anxiety, and a maladaptive style positively associated with anxiety. Primarily cross-sectional studies have shown strong and consistent relationships between catastrophizing, rumination and blaming oneself for what one has experienced and the reporting of anxiety in all age groups and across groups with different cultural backgrounds. To a lesser extent negative relationships have been found between reappraisal, refocusing on pleasant issues and thinking how to handle negative events on the one hand and the reporting of anxiety on the other (Garnefski and Kraaij 2007; Potthoff et al. 2016).

As the use of a predominantly maladaptive cognitive coping style is more strongly related to psychopathology than is the parsimonious use of an adaptive coping style, it might be more beneficial to focus therapy on improving maladaptive cognitive coping strategies rather than enhancing reappraisal and other adaptive coping strategies (Aldao et al. 2010). For example, Krijn (2005; results partially published in Krijn et al. 2007) reports significant reduction in the use of maladaptive coping strategies from pre-treatment to post-treatment in 35 patients following cognitive behavioral therapy (CBT)

for aviophobia, and no changes in the use of adaptive coping strategies; however, she failed to relate these changes to outcome.

Fear of Flying

The present study examined within a group of people with aviophobia the relationship between (changes in) coping style and (changes in) anxiety and avoidance behavior during treatment and at 3-year follow-up. It is estimated that more than a third of all people find flying difficult and distressing. Fear of flying (FOF, aviophobia) is a debilitating disorder affecting 10% - 15% of the general population in the western world (Oakes and Bor 2010a; Ekeberg et al. 2014). Nearly all of these people either avoid flying, or fly with the help of medication, drugs or alcohol. The preferred treatment method is cognitive-behavioral therapy combined with exposure. Acclaimed success rates of therapy range from 67 to 96% (Oakes and Bor 2010b). People with aviophobia seeking treatment are found to have a dispositional tendency towards maladaptive strategies, including avoidance behavior, to cope with their anxiety (Kraaij et al. 2003). In general, phobic people try to avoid both actual and cognitive confrontation with their feared object (Pittig et al. 2014; Sadaat et al. 2014). Cognitive avoidance can be seen as conscious suppression of unwanted thoughts. Such attempts can be counterproductive, leading to increased accessibility of the suppressed thoughts; this then results in hypersensitivity to anxiety-related thoughts and symptoms (Wenzlaff and Wegner 2000). For the present study, we based our analyses on the aggregated adaptive and maladaptive coping styles mentioned above. We included cognitive avoidance among the maladaptive cognitive coping styles.

Hypotheses

Our first study hypothesis was (a) that participants with aviophobia who use maladaptive strategies more often than adaptive strategies at the start of treatment will profit less from treatment. While cognitive coping strategies refer to personal coping styles, these styles are not rigid and therefore amenable to change by targeted intervention (Garnefski and Kraaij 2007). So, we further expected (b) that cognitive-behavioral therapy would result in an enhanced use of adaptive coping strategies, and especially a reduced use of maladaptive coping strategies. Finally, we hypothesized (c) that in particular a reduction of the maladaptive coping style during treatment would predict a better long-term therapy outcome.

METHODS

Participants

The sample in this study comprised 59 adults (28 men) with an average age of 42.3 years (S.D. = 11.0, range 20 – 61). The present study was part of a longitudinal study on psychophysiological aspects associated with fear of flying (Busscher et al. 2015). The original study started with 127 participants who had applied for therapy to overcome their aviophobia. Seventeen participants did not complete therapy. Study dropout from the original study was considerable over the course of time (n = 31) and, once excluded from the original study, study-dropouts were no longer required to fill out the Cognitive Emotion Regulation Questionnaire-Flight (CERQ-F). Consequently 79 participants provided CERQ-F data at the end of treatment (T1). Inclusion criteria for the present study were complete data on the CERQ-F at intake (T0), end of treatment (T1) and at 5-month follow-up (T2). Only 59 of the 79 participants attended this optional short-term follow-up (T2). Therefore, another 20 participants were lost for analysis. All 59 completers provided long-term outcome data at T3 (3 years after short-term follow-up).

MATERIALS

Visual Analogue Flight Anxiety Scale (VAFAS) (Nousi et al., 2008). This single-item one-tailed scale was used to examine to what extent participants were anxious about flying. The scale ranges from 0 (No flight anxiety to 10 (Terrified or extreme flight anxiety).

CERQ-F. The CERQ-F is an adaptation of the 36-item CERQ (Kraaij, Garnefski, & Gerwen, 2003) to measure cognitive coping with flying specifically and was extended by the originators with an additional tenth subscale to assess the use of cognitive avoidance strategies.

This 40 item self-report inventory assesses the following ten conceptually different cognitive coping strategies: 1) Self-blame, thoughts of blaming yourself for what you have experienced; 2) Acceptance, thoughts of accepting what you have experienced and resigning yourself to what has happened; 3) Rumination, thinking about the feelings and thoughts associated with the negative event; 4) Refocus Positive, thinking about joyful and pleasant issues instead of thinking about the actual event; 5) Refocus Planning, thinking about what steps to take and how to handle the negative event; 6) Positive Reappraisal, thoughts attaching a positive meaning to the event in terms of personal

growth; 7) Putting into Perspective, thoughts that play down the seriousness of the event or emphasize its relativity when compared to other events; 8) Catastrophizing, thoughts explicitly emphasizing the terror of an experience; 9) Other-blame, thoughts that put on others the blame for what you have experienced and; 10) Cognitive Avoidance, thinking about how to avoid thoughts of the negative event. All 40 items are rated on a 5-point Likert-type scale ranging from 1 (almost never) to 5 (almost always). The score of a subscale is obtained by adding up the scores of the 4 items belonging to the particular subscale, and it ranges from 4 (never used) to 20 (often used cognitive coping strategy).

The original 36-item CERQ has been used in the study of a wide variety of domains, including depression, anxiety and mental health. Construct validity, reliability, and test-retest reliability of the CERQ proved to be good within subgroups of adolescents, adults, elderly people and psychiatric patients. The inventory has been translated into many languages and shows good cross-cultural consistency. The test-retest correlations of the CERQ indicate that cognitive coping strategies are relatively stable over time, although not as stable as personality traits (Garnefski and Kraaij 2007; Potthoff et al. 2016).

Within the CERQ subscales exists a second order hierarchical structure with two composite subscales (Potthoff et al. 2016). The second order adaptive coping style scale is the simple straight sum of all 12 items from the subscales of Refocus-Positive, Refocus-Planning and Positive-Reappraisal, and ranges from 12 to 60. The 16-item maladaptive coping style scale is the sum score of all items belonging to the subscales of Self-Blame, Rumination, Catastrophizing and Avoidance, and ranges therefore from 16 to 80. The internal consistency of the adaptive and maladaptive scales in the present study was good, with Cronbach's alpha ranging from .85 to .89 for the adaptive scale and from .85 to .88 for the maladaptive scale. For clarity, when referring to the ten different subscales of the CERQ-F we use the term coping strategies, and when referring to the two second order composite subscales we use the term coping styles.

Treatment

Participants in this study followed a highly standardized treatment program for fear of flying at a specialized institution in The Netherlands. The program started with a diagnostic assessment followed by up to four individual 1-hour cognitive behavioral therapeutic sessions (CBT). Then participants joined a two-day cognitive-behavioral group treatment (CBGT), lasting 20 hours in total. A group consisted of an average of eight participants. The second day of CBGT was focused on exposure and included a guided return flight on a commercial airliner. Information on cognitive emotion regulation and

training in coping skills were included in the individual CBT and the group CBGT. Three months after CBGT participants were invited to attend an optional single three-hour follow-up session. Details of the therapeutic protocol have been published elsewhere (Van Gerwen et al. 2006).

Data collection procedure

Coping strategies (CERQ-F) and flight anxiety (VAFAS) were assessed concurrently at three moments in time. Baseline measurements (T0) were integrated into the existing intake before start of treatment. The second assessment (T1) was performed 2 months after baseline, at the end of CBGT. At 5 months after baseline a short-term follow-up assessment (T2) took place during the optional three-hour follow-up session. Three years after short-term follow-up participants furnished long-term effects of therapy (T3) by providing a flight anxiety score (VAFAS) and reporting their number of flights flown within these three years. Email was used to collect this long-term data. CERQ-F data was not collected at T3.

Statistical Analysis

Chi-square tests, independent *t*-tests and one-way ANOVAs were used to examine baseline (T0) and end of treatment (T1) differences in flight anxiety and coping strategies between completers (i.e. participants with a CERQ-F score at T2) and dropouts (those who did not furnish a CERQ-F score at T2). Treatment effects on VAFAS were assessed with paired samples *t*-tests. Changes in coping strategies and coping styles between T0, T1 and T2 were assessed with paired samples *t*-tests.

Multiple regression analyses (MRA) were used to assess the relationship between cognitive coping and long-term treatment effect (T3). Long-term treatment effect was operationalized as the flight anxiety scores three years after short-term follow-up (VAFAS), and number of flights taken in this three-year period. Number of flights was first log (Ln) transformed to obtain a normal distribution. Predictor variables were the scores on the adaptive and maladaptive scales of the CERQ-F at T0, and residualized changes on these scales from baseline to short-term follow-up (T0 – T2). Theoretically, merging separate indicators into composite measures extends the range of scores available and increases power in regression analyses by reducing the number of predictor variables. Preliminary analyses revealed that the use of specific coping strategies continued to change after therapy (T1) up to short-term follow-up (T2). We therefore used the T2 values instead of the T1 values in the MRA on changes in coping style, because these short-term follow-up coping scores best reflected the coping styles used by participants

during the three years after therapy[1]. As anxiety severity and cognitive coping are known to be strongly interrelated, we performed all our analyses with corresponding anxiety scores as covariates in the first step of the analyses. Cognitive coping scores were added in a second step to assess whether they significantly predicted outcome over and above anxiety severity at T0 or changes in anxiety severity between T0 and T2 when appropriate.

Several analyses were performed. To test whether coping styles at baseline were predictive of long-term treatment results, flight anxiety at baseline (VAFAS T0) was entered in the first step of the MRA. The baseline (T0) scores of the adaptive and maladaptive scales were added in a second step. Secondly, we tested whether changes in coping style during treatment until short-term follow-up (T0 – T2) were predictive of changes in flight anxiety from short-term follow-up to three years later (T2 – T3), and in number of flights flown in that period. We calculated residualized change scores and used these throughout the analyses. Changes in flight anxiety during treatment until short-term follow-up (VAFAS T0 – VAFAS T2) were entered in the first step of the MRA and changes in adaptive and maladaptive coping styles during treatment until short-term follow-up (T0 – T2) in the second step. By doing so results from the second step of the MRA indicate the association of changes in coping styles from baseline to short-term follow-up with maintenance of treatment outcome, over and above changes in flight anxiety from baseline to short-term follow-up.

RESULTS

Drop-out Analyses

Statistical analyses showed no significant differences at baseline on demographic and clinical characteristics between treatment dropouts (n=17), study dropouts (n=51) and completers (n=59). Moreover, there were no systematic differences in flight anxiety scores and CERQ-F scores at baseline (T0), and in flight anxiety and CERQ-F scores at T1 (end of treatment), between participants who provided CERQ-F data at T2 (short-term follow-up) and participants who did not do so (data not presented, but available on request).

Clinical characteristics

Socio-demographic characteristics were in line with data previously published on patients applying for therapy at this treatment facility (Busscher et al. 2010). Only 7%

[1] Analyses with T1 values produced similar results.

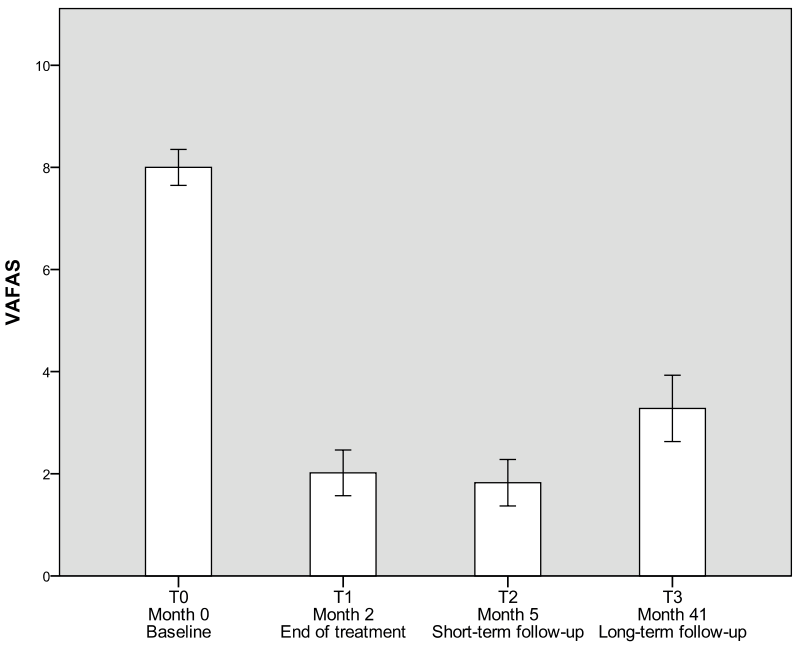

Figure 1. Bar chart of flight anxiety scores (VAFAS) at baseline (T0), end of treatment (T1), short-term follow-up (T2) and long-term follow-up (T3). Error Bars reflect 95% CI. VAFAS = Visual Analogue Flight Anxiety Scale.

of the participants had never flown before start of treatment. Of the participants who had flown before, 32% had flown within 12 months of their application for therapy. The majority, however, had not flown for more than two years, while 29% had not flown for more than ten years. The mean time between application for therapy and the last flight was 5.1 years (SD = 8.1). Figure 1 depicts flight anxiety scores at baseline (T0), end of treatment (T1), short-term follow-up (T2) and three years after short-term follow-up (T3). Cohen's d showed large effect sizes for the reduction in flight anxiety between baseline and all other measurement moments, ranging from 4.0 at short-term follow-up to 2.6 at long-term follow-up.

CERQ-F strategies

Table 1 shows values for the 10 subscales of the CERQ-F at the different assessment moments. Significant changes were seen over time in adaptive and maladaptive strategies. The maladaptive coping strategies Self-Blame, Rumination, Catastrophizing

Table 1. Cognitive strategies and cognitive style at baseline, end of treatment and short-term follow-up.

	T0	T1	T2	T0-T1		T1-T2		T0-T2	
Coping strategy				*p*	*Cohen's d*	*p*	*Cohen's d*	*p*	*Cohen's d*
Self-blame	11.93 (3.3)	9.17 (3.2)	8.17 (3.3)	< .001	.85	.027	.31	< .001	1.14
Acceptance	10.76 (2.7)	10.85 (3.5)	10.42 (3.6)	.724	.03	.326	.12	.550	.11
Rumination	12.83 (3.0)	10.31 (3.0)	9.39 (2.9)	< .001	.84	.023	.31	< .001	1.17
Refocus positive	7.34 (3.1)	10.33 (3.3)	10.27 (2.9)	< .001	.93	.727	.02	< .001	.98
Refocus planning	10.67 (3.2)	12.63 (3.9)	11.51 (3.0)	.003	.55	.025	.32	.143	.27
Positive reappraisal	7.78 (3.5)	13.39 (2.9)	12.12 (3.3)	< .001	1.75	.018	.41	< .001	1.28
Putting into perspective	7.05 (2.9)	10.74 (3.7)	9.08 (3.6)	< .001	1.11	.002	.45	< .001	.62
Catastrophizing	10.10 (3.8)	6.06 (2.9)	5.20 (2.0)	< .001	1.20	.051	.35	< .001	1.61
Other blame	5.47 (2.2)	4.81 (2.0)	4.59 (1.5)	.049	.31	.596	.12	.003	.47
Avoidance	10.93 (4.4)	5.52 (2.5)	5.12 (1.9)	< .001	1.51	.358	.18	< .001	1.71
Coping style				*p*	*Cohen's d*	*p*	*Cohen's d*	*p*	*Cohen's d*
Adaptive	25.88 (7.7)	36.35 (8.2)	33.90 (7.3)	< .001	1.32	.037	.32	< .001	1.07
Maladaptive	45.79 (10.5)	31.06 (8.5)	27.88 (8.0)	< .001	1.54	.015	.39	< .001	1.92

T0 = baseline. T1 = end of treatment. T2 = short-term follow-up. Between brackets: standard deviation.

and Avoidance were used significantly less often at the end of treatment (T1) and short-term follow-up (T2) as compared to baseline (T0). The adaptive coping strategies Refocus-Positive and Positive-Reappraisal were used significantly more often at T1 and T2 as compared to T0. Refocus Planning as coping strategy was used significantly more often at T1 than at T0, but the t-test between baseline (T0) and short-term follow-up (T2) was not significant. Effect size statistics showed large effect for 6 out of 10 strategies, with catastrophizing and avoidance paramount, Cohen's d 1.61 and 1.71 respectively. Participants showed clinically significant improvement in cognitive coping strategies, from pre-treatment scores matching those of dysfunctional populations to post-treatment responses matching those of a normal population.

Adaptive and Maladaptive coping styles

Table 1 also shows values for the adaptive and maladaptive styles at the different assessment moments. Using paired *t*-tests we found a significant persistent decline in the use of the maladaptive coping style from baseline to T1 and T2. In contrast, for the adaptive scale we found a significant increase from baseline to T1, followed by a significant decrease from T1 to T2. Still, on the adaptive scale participants had a significantly higher score at T2 than at T0. Cohen's d indicated large changes on both scales, with greater changes on the maladaptive than on the adaptive scale.

Prediction of outcome by cognitive coping at baseline

Multiple regression analyses were performed to examine whether long-term therapy outcome (T3) could be predicted by coping styles at baseline (T0). The adaptive and maladaptive coping styles at the start of therapy showed no significant relationship with long-term treatment outcome (Tables 2 and 3).

Long-term maintenance of flight anxiety by changes in coping style during treatment

Changes in coping style during treatment until short-term follow-up (T0 – T2) were predictive of changes in flight anxiety from short-term follow-up to three years later (T2 – T3). The additional explained variance in flight anxiety by changes in adaptive and maladaptive coping style over and above changes in flight anxiety (T0 – T2) during treatment was 21%. As shown in Table 2, this effect was brought about predominantly by changes in maladaptive style. Participants with a greater decrease in the use of the maladaptive coping style reported less increase in flight anxiety from short-term follow-up to 3 years later than did participants who had less decrease in the maladaptive coping style.

Prediction of number of flights by changes in coping style during treatment

In the three years after therapy (T3), participants flew on average 12.4 flights (SD 12.1). Only 2 participants did not fly, one participant reported 70 flights in this 3-year period. As shown in Table 3, the additional explained variance of flights taken by changes in adaptive and maladaptive coping style over changes in flight anxiety was 12%. Participants with a greater increase in the use of the adaptive coping style reported more flights than did participants with less increase in the use of the adaptive coping style. Participants with a greater decrease in the use of the maladaptive coping style flew more often than did participants who had less decrease in the maladaptive coping style during therapy.

Table 2. Prediction of long-term therapy outcome (Flight Anxiety; VAFAS at T3) by adaptive and maladaptive coping styles at baseline (To), and prediction of long-term maintenance of flight anxiety (VAFAS T2 – VAFAS T3) by changes in adaptive and maladaptive coping styles from baseline (To) to short-term follow-up (T2).

	Beta	*SE*	*t*	*p*	Zero-order correlation	*R*	R-Square
Flight Anxiety at T3			**Baseline (To)**				
Step 1						.007	.000
Flight Anxiety (To)	.007	.275	.051	.960	.007		
Step 2						.181	.033
Flight Anxiety (To)	-.009	.277	-.063	.950	.007		
Adaptive coping (To)	-.039	.043	-.269	.789	-.047		
Maladaptive coping (To)	.176	.034	1.19	.240	.176		
Maintenance of flight anxiety (T2 – T3)			**Changes in Coping Styles (To – T2)**				
Step 1						.017	.000
Flight Anxiety (To – T2)	.017	.150	.113	.910	.017		
Step 2						.461	.214
Flight Anxiety (To – T2)	-.213	.155	-1.38	.174	.017		
Adaptive (To – T2)	.037	.130	.261	.795	.177		
Maladaptive (To – T2)	.505	.151	3.16	.003	.418		

To = baseline. T2 = short-term follow-up. T3 = 3 years after short-term follow-up.

Table 3. Prediction of long-term therapy outcome (Number of Flights) by adaptive and maladaptive coping styles at baseline (To), and by changes in adaptive and maladaptive coping styles from baseline to short-term follow-up (T2).

	Beta	***SE***	***t***	***p***	**Zero-order correlation**	***R***	**R-Square**
Number of Flights				**Baseline (To)**			
Step 1						.120	.014
Flight Anxiety (To)	-.120	.089	-.831	.410	-.120		
Step 2						.181	.033
Flight Anxiety (To)	-.122	.092	-.808	.423	-.120		
Adaptive coping (To)	-.133	.016	-.906	.370	-.137		
Maladaptive coping (To)	.020	.012	.132	.895	-.001		
Number of Flights				**Changes in Coping Styles (To – T2)**			
Step 1						.275	.076
Flight Anxiety (To – T2)	-.275	.127	-1.94	.058	-.275		
Step 2						.439	.193
Flight Anxiety (To – T2)	-.117	.139	-.759	.452	-.275		
Adaptive (To – T2)	.290	.116	2.03	.048	.206		
Maladaptive (To – T2)	-.329	.136	-2.05	.046	-.306		

To = baseline. T2 = 3-month follow-up. T3 = 3 years after short-term follow-up.

DISCUSSION

The present study examined, within a relatively large clinical sample of people with aviophobia, the predictive value of using cognitive coping strategies at pre-treatment and of changes in these strategies during treatment for long-term therapy results. Results indicated that participants were in a long-term process of change, which in the case of maladaptive cognitive coping strategies continued positively after therapy; this was not the case for adaptive strategies. The use of cognitive coping strategies at baseline was not predictive of therapy outcome. However, a greater increase in the use of adaptive coping strategies, and more importantly, a greater decrease in the use of maladaptive coping strategies during therapy were indicative for less long-term relapse of flight anxiety and more flights flown. The most important significant predictor of maintenance of treatment gains, therefore, was reduced use of a maladaptive coping style over therapy. In general, within anxiety pathologies the use of the maladaptive coping style seems to play a more prominent role in cognitive emotion regulation than does the adaptive coping style (Garnefski and Kraaij 2007; Aldao et al. 2010; Omran 2011; Rooij et al. 2014). Our findings reinforce the idea that the preponderant presence of a maladaptive coping style might be more detrimental than the relative absence of an adaptive coping style, and that improving maladaptive emotional cognitions during therapy might be more beneficial than improving reappraisal and other adaptive coping strategies.

Maladaptive strategies predominate over adaptive strategies

The beneficial use of generally adaptive strategies might be more context-dependent, and seem to work less well in situations perceived as uncontrollable, as when traveling in an airplane (Cruess et al. 2002; Aldao et al. 2010). For example, when strapped in a seat during a turbulent flight it might be difficult to attach a positive meaning to the event in terms of personal growth (reappraise), or think about joyful and pleasant issues instead of the actual event (refocus positive). Instead, cognitive avoidance, emphasizing the terror of an experience (catastrophizing) and thinking about the feelings and thoughts associated with the negative event (rumination) might even seem perfectly appropriate in this uncontrollable and frightening situation. The lack of control seems to favour the predominant use of maladaptive strategies. Furthermore, the use of one maladaptive strategy to deal with a negative event evokes the use of other maladaptive strategies. Rumination without reappraisal will easily lead to catastrophizing and avoidance. This self-reinforcing process favoring maladaptive strategies might override attempts to use more adaptive strategies.

Implications

Because maladaptive cognitive coping and emotion regulation strategies can be seen as transdiagnostic factors associated with various psychopathologies such as anxiety, depression and eating disorders, interventions focusing on these factors may have positive effects across a range of disorders (Aldao et al. 2010). A myriad of techniques is available (Mennin et al. 2013). Most cognitive behavioral therapies are heterogeneous and make use of multiple traditional and newer components such as cognitive reframing, behavioral exposure, behavioral activation, decentering, attention training and acceptance/tolerance. These therapies can be seen as a blunt instrument that by its heterogeneous nature effectively targets maladaptive coping strategies without concern as to which precise ingredient causes which outcome (Dobson 2013; Hofmann et al. 2013; Mennin et al. 2013). Also in the present study it remains unclear to what extent cognitive interventions such as psychoeducation or in vitro exposure or behavioral interventions such as exposure in the form of a guided flight contributed to reductions in catastrophizing, cognitive avoidance, rumination and self-blame. Delineating and empirically evaluating treatment components that critically affect the use of certain maladaptive cognitive coping strategies could help to make treatment programs more parsimonious and effective. More effectively targeting specific maladaptive cognitive coping strategies would be greatly enhanced by a more refined knowledge of the functional relationships between certain therapy ingredients and maladaptive coping strategies.

Strength and limitations

The strength of the present study is its use, within a clinical sample of people with aviophobia, of two entirely different clinically relevant long-term outcome measures: a self-report measure indicating flight anxiety and a behavioral measure indicating flight behavior. Another positive point of the study is its longitudinal design with multiple concurrent assessment moments of coping strategies and flight anxiety. Coping strategies were, however, not assessed at long-term follow-up, thus precluding a cross-lagged panel analysis and formal mediation analysis. Although we could not establish that changes in cognitive coping preceded changes in flight anxiety during active treatment, we did establish that changes in cognitive coping during treatment were predictive for long-term treatment outcome, over and above changes in flight anxiety during treatment. To our knowledge this is the first study to report the predictive values of changes in maladaptive coping strategies during treatment for subsequent clinical change within the anxiety domain. These results warrant future controlled studies with repeated measurements of anxiety and cognitive coping in order to formally test the mediating role of changes in cognitive coping.

We must also acknowledge some study limitations. The present study was conducted at a specialized treatment facility, not a research facility. Participants were highly anxious aviophobics who applied for treatment, and paid for their treatment. This setting limited research and assessment options considerable. Consequently, follow-up assessment was restricted to flight anxiety and flight behavior. The present study did not include a control condition, but the considerable changes in flight anxiety and cognitive coping during treatment make it unlikely that these changes in a sample with protracted complaints are the results of passage of time or repeated testing. Participants in the present study followed CBT with cognitive therapy preceding behavioral components, including two exposure flights. Although appealing from a theoretical perspective, the congruent changes in cognitive coping strategies and flight anxiety during treatment do not necessarily imply a causal relationship. Other mechanisms of change, like exposure, could have led to anxiety reductions and consecutive changes in the use of coping strategies. Recently it has been proposed that consolidation of treatment progress could benefit from post-exposure cognitive interventions, instead of pre-exposure cognitive therapy (Craske et al. 2014; Busscher et al. 2015). Randomized controlled trials are needed to test this assumption.

Another study limitation is that flight behavior is not only contingent on fear of flying but is also influenced by financial aspects as well as work, family and peer pressure. True as this may be, the clinically important aspect here is that participants, who did not fly in years before therapy, flew on average 12 flights in the three years after therapy. Finally, study attrition may limit generalizability of study findings, although there were no significant differences in baseline characteristics between completers and dropouts.

CONCLUSION

Diminishing the use of self-blame, rumination, catastrophizing and avoidance as coping strategies might be a key mechanism of change for people with aviophobia. Multiple coping strategies are used simultaneously, and a cognitive coping strategy that is appropriate in one situation might be less useful in another situation (Doron et al. 2013). The context of the situation may dictate which coping strategies could best be used, while a flexible use of several strategies dependent on the context could be most useful. The beneficial use of generally adaptive strategies seems to work less well in situations that are perceived as uncontrollable, such as traveling in an airplane (Cruess et al. 2002; Aldao et al. 2010). Cognitive interventions for aviophobia should therefore primarily target the maladaptive coping strategies.

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5

Chapter 6

Psychological distress and physiological reactivity during in vivo exposure in people with aviophobia

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ABSTRACT

Objective: Exposure is regarded to be a crucial component of therapies for phobias. According to Emotional Processing Theory (EPT), the success of exposure therapy is predicted by activation of subjective and physiological fear responses and their within-session habituation and between-session adaptation. This study tested this prediction for aviophobia.

Methods: Seventy-nine participants following a highly standardised treatment program for aviophobia provided self-reported and physiological (heart rate, respiratory sinus arrhythmia and pre-ejection period) measurements of fear activation, within-session habituation and between-session adaptation during exposure to flight-related stimuli, a flight simulator, and during two real flights. Multiple regression analyses were conducted to examine whether these measurements predicted therapy outcome up to 3 years after finishing therapy, including number of flights flown in this period.

Results: Both subjective and physiological arousal measurements indicated strong fear activation and large within-session habituation and between-session adaptation during exposure. Flight-anxiety measures showed large improvements up to three years after treatment (η^2 between .72 - .91). Lower self-reported anxiety during flight exposure was associated with lower flight-anxiety after exposure (R^2 = .15) and more flights flown (R^2 = .14). Within-flight habituation or between-session adaptation of self-reported anxiety had no relationship with treatment outcome. Within-flight habituation of HR reactivity (R^2 = .10) and respiratory sinus arrhythmia reactivity (R^2 = .11) was associated with lower flight-anxiety directly after the flight, but not on flight-anxiety three years after finishing therapy or on long-term flying behaviour.

Conclusions: The results provide only weak support for Emotional Processing Theory. Low self-reported anxiety during in-vivo flight exposure was the best predictor of successful long-term therapy outcome.

INTRODUCTION

A third of the general population in the western world has trouble flying without worries, and again one third of this group does not fly at all (1, 2). Yet only a few of all those people face their fear and start therapy. Although highly efficacious on the short term (3), little is known about therapy effectiveness in the long run. Fear of Flying (FOF) is a heterogeneous phenomenon and often includes, or is a combination of, acrophobia, claustrophobia, fear of losing control, fear of a crash, and panic and social phobias. Although classified as a specific phobia, also known as simple phobia, fear of flying is far from simple in view of the heterogeneous and compound nature of this phobia. This is mirrored in the divergent outcomes of the studies on this subject (1, 2, 4-6). Especially the physiological reactivity to flight-stressors is complex (7-17). Therapy often tackles the multitude of underlying phenomena with a combination of providing information, cognitive restructuring, relaxation training and graded exposure (2, 3). The latter exposure is often regarded as the crucial component of therapies for phobias and other anxiety disorders. According to emotional processing theory (EPT), exposure to the feared stimulus activates the fear network, and activation of this fear network is seen as a necessary condition for improvement (18). The concept of a fear network stems originally from Lang (19) and Rachman (20). "Fear structures" within the fear network comprise of a "network" of stimulus (e.g. turbulence), response (e.g. racing heart) and meaning (e.g. we will crash, I will die) components. Activating any part of the fear structure (e.g. a racing heart) will generalize to activate other parts of the structure (18, 19, 21, 22). Emotional processing involves incorporating new information into an existing fear structure, allowing for both a decrease and an increase in the emotional response. Integration of new information that is incompatible with the existing fear structure will reduce fear by replacing (18) or competing with (23) the original fear structure.

According to EPT, successful emotional processing is indicated by within-session habituation of fear responses, reflected in reduced subjective anxiety and physiological arousal during exposure. Although ample evidence exists for beneficial effects of treatment on within-session habituation, there is only scant evidence to suggest that this within-session habituation translates into long-term treatment outcome (22, 24). Beneficial effects of treatment on the adaptation of subjective anxiety and physiological arousal across multiple exposures are the second indication of successful emotional processing expected by EPT. This between-session adaptation is believed to involve higher levels of cognitive operations and long-term habituation (or extinction, but to avoid confusion we conform to the EPT convention and use habituation throughout

the paper) by means of evaluative learning (21, 24). Most studies on different phobic behaviors find support for a positive relationship between between-session adaptation and long-term treatment outcome (for an overview see 22). However, some report little (21) or no predictive value of between-session adaptation for treatment outcome (25). To our knowledge no research on the relationship of between-session adaptation and outcome has been published within the framework of fear of flying.

In this study we report on both subjective and physiological reactivity in individuals with fear of flying to flight-related stimuli and to real-flight. A large sample of aviophobics who applied for therapy was followed up from diagnostic assessment up to three years after finishing therapy to examine how their fear of flying and actual long-term flight behavior were affected by treatment. We first assessed fear activation as the increase in self-reported anxiety and physiological arousal during exposure to flight-anxiety inducing videos, a flight simulator and two real flights. Secondly, we assessed whether within-session habituation and between-session adaptation of self-reported anxiety and physiological arousal predicted the short and long-term effects of exposure therapy. Flight anxiety scores taken directly after two exposure flights were used as an indication for short-term effect. Flight anxiety three years after finishing therapy, and the number of flights taken in this three-year period were used as an indication of long-term effects. We predicted better therapy outcome (less flight anxiety, more flights) for participants with a more pronounced activation of the fear network during exposure, with a higher within-session habituation during exposure and a larger between-session adaptation. Furthermore, we expected that the prediction of therapy outcome would be improved by adding measurements of physiological reactivity to self-report of anxiety.

METHODS AND MATERIALS

Participants

The 79 participants (37 men) with an average age of 40.4 (S.D. = 11.0, range from 20 to 61 years) in this study were aviophobics, who participated in a cognitive-behavioral group treatment (CBGT) to overcome their fear of flying. Most participants were self-referrals. Health care agencies, health care professionals and company health programs referred a minority of participants. Airline personnel were excluded from this study. Other reasons for exclusion were current use of cardioactive medication like β blockers, pharmacotherapeutic medication and a concurrent panic disorder of such severity according to the treating psychotherapist that it would seriously interfere with the

treatment of fear of flying. Inclusion criteria were a good understanding of the Dutch language and no flight scheduled before end of the CBGT. Written informed consent was obtained from all participants before the start of the diagnostic process. The Leiden University Medical Center medical ethics committee approved the research protocol.

Therapeutic procedure

Participants in this study followed a highly standardized treatment program for fear of flying at the VALK foundation in The Netherlands, as described in detail elsewhere (6). Briefly, the fear of flying program starts with a diagnostic assessment, followed by individual therapeutic sessions covering relaxation and breathing techniques, psychological factors involved in fear and anxiety, and coping skills. Claustrophobia, acrophobia, traumatic transportation accidents and traumatic social events were addressed if applicable. Participants started a two-day cognitive-behavioral group treatment (CBGT) within 5 weeks from diagnostic assessment. The first day of group treatment offered technical information on flying and psycho-education. The second day of CBGT started with cognitive training. The afternoon focused on exposure and included in vivo exposure to two simulated flights in a full motion cabin flight simulator normally used for cabin crew flight safety training and two real flights on a commercial airliner.

Data Collection Procedure

Before the start of the diagnostic assessment, before each individual therapeutic session, and at the beginning of both days of CBGT, an ambulatory monitoring device was attached to record changes in physiological arousal. During all visits to the VALK facility, and the first day of CBGT, subjects were regularly exposed to an anxiety inducing flight video. The flight video was preceded by a neutral video. Different videos, each lasting six minutes, were used on each repetition. Video exposure moments were before the start of the diagnostic phase, at the end of each individual session and three times during the first day of CBGT. Subjective units of distress (SUD) were measured directly after neutral and flight video presentations. On the second day of CBGT, SUD's were collected midway in the morning program (shortly before the start of the in-vivo exposure), directly after both simulator flights and during both flights directly after doors closed, during cruise flight and after landing before doors open. The day after the exposure flights, data was analysed off-line. The ambulatory monitoring device has an event marker and a built-in vertical accelerometer. Both the therapist and the accompanying pilot kept a detailed log during both flights. All these resources were used to select movement-free and artefact-free periods that lasted at least 5 minutes each around the times the SUDs were collected. Physiological reactivity scores were computed based on these 5-minute periods

to ensure the temporal overlap of the subjective and physiological measurements of fear activation. After disembarkation, participants filled out questionnaires on flight phobia. Thereafter, the ambulatory recording device and electrodes were removed. Post-treatment flight anxiety data were collected at three months and one year after CBGT. Participants furnished long-term effects of therapy by providing a flight anxiety score three years after therapy, and the number of flights flown within these three years. Data collection was from October 2006 to October 2010. The entire timeline for the data collection, therapeutic and follow-up procedure is captured in figure 1.

Physiological recordings

Heart Rate (HR), Respiratory Sinus Arrhythmia (RSA) and the Pre-Ejection Period (PEP) were recorded using the VU-AMS (version 4.6, Vrije Universiteit Amsterdam, The Netherlands; www.vu-ams.nl). The VU-AMS is a lightweight ambulatory device that unobtrusively records the electrocardiogram (ECG) and impedance cardiogram (ICG) continuously by means of six Ag-AgCl electrodes attached to the torso region (26, 27). Subjects habituate easily to the device while maintaining full freedom of motion. The apparatus has an event marker and a built-in vertical accelerometer, which output can be used to select movement free periods for analysis. RSA is a measure of parasympathetic control (28), whereas PEP is considered a measure of sympathetic cardiac control (29). Scoring of these variables was automatic, followed by visual inspection of the impedance and respiratory signal from the entire recording. Details on scoring of these variables, recording methodology, reliability and validity are described elsewhere (30, 31). Briefly, from the ECG (sampling rate 1000 Hz) the HR was obtained from the time between two adjacent R waves. PEP was defined from the ECG and ICG as the time interval from the Q-wave onset, the onset of the electromechanical systole, to the B-point (from the ICG), which signals opening of the aortic valves (27, 29). RSA was obtained from the ECG and thorax impedance derived respiration signals by subtracting the shortest interbeat interval during HR acceleration in the inspirational phase from the longest interbeat interval during deceleration in the expirational phase (i.e. the peak-through method) (32). When no phase-related acceleration or deceleration was found, the breath was assigned a RSA score of zero. Fear responses are characterized by increases in HR, shortening of the PEP and decrease in RSA.

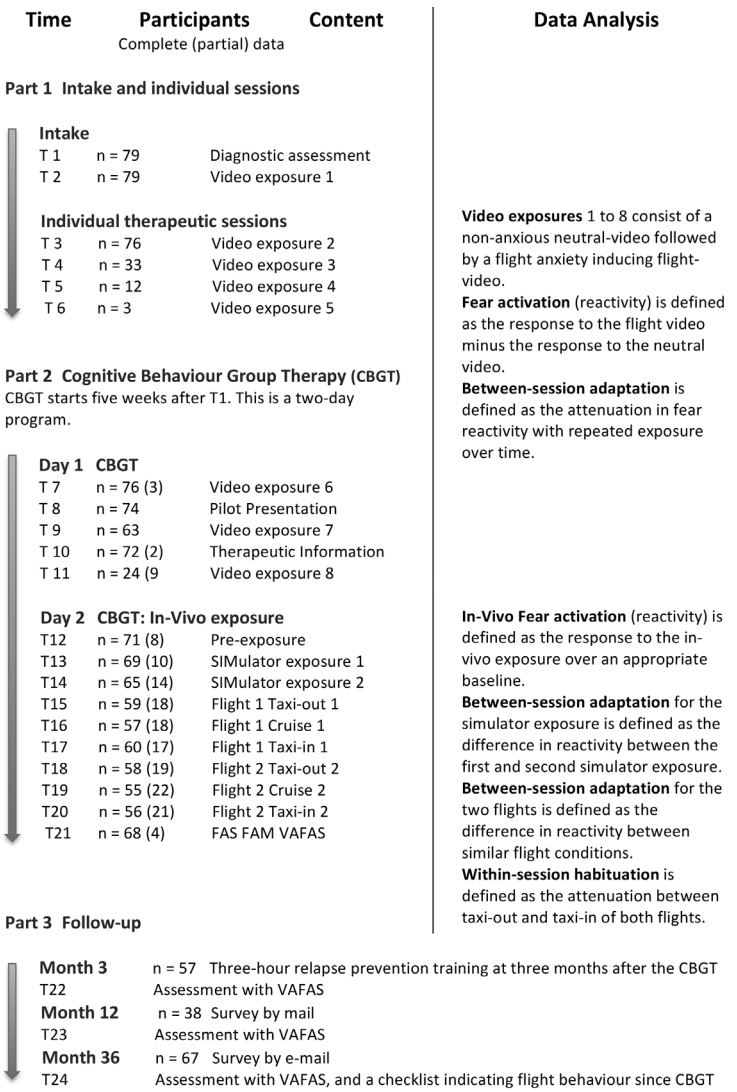

Figure 1. Schematic representation of the data collection and therapeutic and follow-up procedures with information on data loss and data analysis. Data analysis conveys definitions of reactivity scores for video exposure and for in-vivo exposure. Data loss indicates the number of participants furnishing complete data at these moments. Between brackets is the number of participants furnishing incomplete data. Mainly one or more electrodes not recording properly caused data loss during in-vivo exposure. FAS = Flight Anxiety Situations questionnaire, FAM = Flight Anxiety Modality questionnaire, VAFAS = Visual Analogue Flight Anxiety Scale, CBGT = Cognitive Behavioral Group Therapy.

QUESTIONNAIRES

VAFAS

The single-item one-tailed Visual Analogue Flight Anxiety Scale (VAFAS) was used to examine to what extent participants were anxious about flying. The scale ranges from 0 ("No flight anxiety") to 10 ("Terrified or extreme flight anxiety") (33).

SUD

The Subjective Units of Distress (SUD) scale was used to examine to what extent participants were feeling anxious at several moments. Participants had to indicate their perceived anxiety on a one-tailed scale from 1 ("totally relaxed") to 10 ("extremely anxious") (34).

FAS

The Flight Anxiety Situations (FAS) questionnaire assesses anxiety related to flying experienced in different flight or flight related situations. The 32-item self-report inventory uses five point Likert-type scales. The FAS consists of three subscales: (a) an Anticipatory Flight Anxiety Scale, assessing anxiety experienced when anticipating a flight, (b) an In-Flight Anxiety Scale, measuring anxiety experienced during a flight and (c) a Generalized Flight Anxiety Scale, assessing anxiety experienced in connection with airplanes in general (33, 35). The internal consistency of the subscales of the FAS in the present study was good to excellent, Cronbach's Alpha ranging from .77 to .95.

FAM

The Flight Anxiety Modality (FAM) questionnaire is an 18 item self-report inventory that was used to assess the symptoms by which flying related anxiety was expressed. Each symptom is rated on a 5-point Likert-type scale. The FAM consists of two subscales: (a) a Somatic Modality scale, pertaining to physical symptoms and (b) a Cognitive Modality scale, related to the presence of distressing cognitions (33, 35). The internal consistency of the two subscales of the FAM in the present study was good to excellent, Cronbach's Alpha ranging from .74 to .91.

Fear activation, within-session habituation and between-session adaptation

To quantify individual differences in fear activation during exposure to the phobic stimuli we used the changes in subjective distress scores and physiological arousal over an appropriate baseline in a sitting posture. For the video exposure, reactivity scores for each of the three physiological variables (HR, RSA and PEP) and the SUD variable were

created that reflected the response to the flight video compared to the neutral video. The baseline used to compute fear activation for the pre in-vivo exposure period, for both simulated flights and both exposure flights during the second day of CBGT, consisted of the average of all non-fearful conditions during the morning program of the first day of CBGT. Baseline for SUD was defined as the average SUD value reported halfway through the morning program in combination with the SUDs reported directly after the first and second neutral video presentations. For the three physiological variables baseline was the average of the morning program of the first day of CBGT excluding the flight videos, so encompassing both neutral videos and the pilot presentation. In support of the averaging steps, ANOVA showed no significant differences in SUD, HR, PEP or RSA across these separate conditions constituting the baseline (data not presented, but available on request).

Within-session habituation scores were created for the two flights separately by subtracting the reactivity at the end of the flight (Taxi-In) from the reactivity at the start of the flight (Taxi-Out). For the SUD this reflects the decrease in subjective distress in the course of a flight. For HR, RSA and PEP this reflects the decrease in physiological arousal in the course of a flight.

Between-session adaptation for the video stimuli was operationalized as the attenuation in reactivity with repeated exposure over time. Between-session adaptation for the simulator was obtained by subtracting reactivity from the second simulated flight from reactivity to the first simulated flight. Likewise, for real flight between-session adaptation scores were created for taxi-out, cruise, taxi-in by subtracting reactivity to the second flight from reactivity to the first flight. For instance, for subjective distress at taxi-out, between-session adaptation reflects the decrease in SUD reactivity from taxiing-out during the first to taxiing-out during the second flight. Figure 1 provides a schematic representation of fear activation, within-session habituation and between-session adaptation.

Therapy outcome

Short-term effect of therapy outcome was operationalized as the flight anxiety score taken just after both exposure flights (VAFAS post-flight). Long-term effect of therapy outcome was operationalized as the flight anxiety scores three years after treatment, and number of flights taken in this three-year period.

Missing data

Participants in this study were not a homogeneous group. Several participants had never flown before. Some had made more than 25 return flights before onset of their phobia. While most participants needed only one or two sessions, three participants did not require any preparatory sessions before start of the CBGT. Twelve participated in the third individual therapeutic session, and just three participants needed all four therapeutic sessions. The low number of participants during the third and fourth individual therapeutic session severely restricted meaningful conclusions on the video responses during these sessions. We therefore excluded these sessions from the analyses of the video responses. Missing data analysis showed no systematic differences in the video responses to the first two sessions for participants who participated in more than two individual sessions and participants who attended two or fewer individual therapeutic sessions. Because of scheduling conflicts, a few participants were unable to attend to video presentations during the first or second individual sessions. Because of time constraints not all participants viewed the third video presentation at the end of the first day of CBGT. This led to the adoption of MIXED ANOVA RM as the main analysis strategy as it handles missing cells in repeated measures data without removing subjects.

One flight was cancelled due to adverse weather, resulting in the loss of flight-data of two participants. All other participants furnished subjective data during both days of CBGT, including both flights. Physiological data of two participants was lost due to equipment failure during flight. The security checks at the airports were a major challenge for the physiological measurements. The electrodes of the ambulatory measurement device required a physical patting down of all participants, after security screening 19% of the recording devices did not record one or more variables properly during one or both flights. In total, 55 participants provided uncorrupted physiological data at all flight phases, while another 20 participants furnished partially usable physiological data. Figure 1 depicts loss of data at the different times.

Long-term effect of therapy outcome was operationalized as the flight anxiety scores three months, one year and three years after treatment, and number of flights taken in this three-year period. However, only 57 out of 79 participants attended the follow-up session three months after CBGT, and a mere 38 participants returned written questionnaires one year after therapy. Response rate (n=67) three years after CBGT was considerably higher when we used email for data collection. Consequently, analysis of long-term effect of therapy was restricted to the three-year follow-up data from these 67 participants. Missing data analysis on all physiological data and all questionnaire data

available revealed no systematic differences between completers and the participants lost to follow-up.

Data Analysis

RSA and Number of Flights Flown within three years of end of therapy were log (Ln) transformed to obtain normal distributions. Video reactivity was analyzed by means of MIXED ANOVA repeated measures analyses, with time of assessment (time) and condition (neutral video or flight video) as fixed repeated measures factors. Fear activation is reflected in the significance of the condition main effect. Between-session adaptation is reflected in significance of the interaction of time with condition. Repeated measures MIXED ANOVA with condition (baseline, sim1, sim2, flight1 taxi-out, flight1 cruise, flight1 taxi-in, flight2 taxi-out, flight2 cruise, flight2 taxi-in) were used to analyse the in-vivo reactivity during the second day of CBGT. Omnibus significance of the condition effect was followed by post-hoc inspection of reactivity to the individual conditions (i.e. the difference between exposures and the baseline) to test fear activation in these conditions. Between-session adaptation was tested by planned contrasts of the reactivity to both simulator flights (T13-T14) and reactivity to similar conditions during both real flights (T15-T18, T16-T19, T17-T20). Within-session habituation was tested by comparing reactivity to taxi-out and taxi-in during both flights (T15-T17 and T18-T20). The significance level was set at .01.

Multiple regression analyses were used to assess whether fear activation, within-session habituation and between-session adaptation of self-reported anxiety and physiological arousal predicted the short and long-term effects of exposure therapy. Predictor variables were the reactivity scores reflecting fear activation, and the contrasts between reactivity scores reflecting within-session habituation and between-session adaptation as outlined previously. Outcome variables were the short-term and long-term effects on fear of flying and actual flight behaviour. Reactivity, habituation and adaptation scores with a zero-order correlation with $p \leq .01$ were included into the regression equations. Such full models are in agreement with the Journals guidelines. Although the use of full models avoids selection bias, these models are often large and complicated (36). In view of the large number of predictive variables, and to safeguard against overfitting and underfitting, in a secondary analysis redundant predictors were removed by means of bidirectional elimination based on maximizing the adjusted R-Square, that is, mainly removing items with a high mutual correlation and low semi-partial correlation (36-40). As nearly identical results were obtained compared to the full model, we report on the latter analysis only.

RESULTS

Clinical characteristics

On average participants received 1.7 (S.D. = .9) individual therapeutic sessions between the diagnostic assessment and start of the CBGT. Three participants did not require any preparatory sessions before start of the CBGT while only three participants needed all four therapeutic sessions. Table 1 depicts FAS and FAM scores at assessment and post-flight. Eta square (η^2), the effect size statistic for repeated measures ANOVA, showed a large effect for all measures. All values were in line with the established range for these questionnaires (33, 41).

Table 1. Measures of flight-related anxiety at assessment (n = 79) and post-flight (n = 72)

	Assessment score		Post-flight score		
	Mean	SD	Mean	SD	Effect size η^2
FAS					
Anticipatory anxiety	43.4	8.8	24.6	13.9	.60
In-flight anxiety	37.4	8.1	19.4	7.2	.82
Generalized flight anxiety	13.1	4.6	9.1	2.5	.46
Sum score	104.4	18.3	58.9	20.8	.79
FAM					
Somatic complaints	25.8	8.9	15.7	4.4	.65
Cognitive complaints	24.4	7.4	11.7	5.0	.75

Post-flight scores differ from assessment scores at $p < .001$
FAS = Flight Anxiety Situations Questionnaire, FAM = Flight Anxiety Modality Questionnaire, SD = Standard Deviation, η^2 = Eta square, the effect size statistic for repeated measures ANOVA.

Video exposure

Fear activation

Table 2 shows values for SUD and all three physiological variables at the different times of assessment. For the SUD variable a significant condition effect (neutral – flight) was found [$F(1, 88.9) = 94.2$, $p < .001$, mean difference 1.1, 95% confidence interval 1.3 - 0.88]. Post-hoc analyses of the condition effect revealed that participants reported significantly more distress to a flight video than to a neutral video at all measurement moments. Of

the physiological variables only RSA showed a significant condition effect [F(1, 134.6) = 4.1, p = .004, mean difference .054, 95% confidence interval 0.02 - 0.09]. Five of six times participants had significant shorter RSA values (less parasympathetic control) during the flight video compared to the neutral video.

Between-session adaptation

For the SUD variable a significant time-by-condition interaction [F(5, 58.8) = 3.5, p = .008] was found that was caused entirely by a peak response to the first video exposure at the diagnostic assessment (T2), as can be seen in figure 2. RSA showed no significant time-by-condition interaction effect [F(5, 128.7) = 2.5, p = .034]. Because HR and PEP reactivity to the flight videos were non-significant, no between-session adaptation analyses were performed.

Table 2. Mean (SD) of SUD, HR, RSA and PEP during neutral- and flight-video presentations.

Type of Video	SUD	HR(bpm)	RSA(msec)	PEP(msec)
Neutral Video T2	2.6 (1.4)	72.0 (11.7)	51.3 (33.7)	93.0 (16.0)
Flight Video T2	4.0 (1.8)	71.9 (10.2)	48.3 (27.0)	93.5 (16.6)
Neutral Video T3	2.2 (1.3)	67.8 (11.6)	48.3 (30.5)	108.7 (22.4)
Flight Video T3	3.3 (1.6)	68.1 (10.6)	48.5 (27.5)	110.7 (22.5)
Neutral Video T4	2.1 (1.0)	70.4 (9.4)	43.2 (21.9)	96.5 (19.1)
Flight Video T4	3.4 (1.7)	70.3 (8.8)	39.8 (21.5)	95.7 (21.7)
Neutral Video T7	2.6 (1.5)	74.4 (12.1)	43.5 (31.9)	101.3 (21.0)
Flight Video T7	3.5 (1.6)	74.3 (11.7)	43.3 (27.8)	101.6 (21.5)
Neutral Video T9	2.1 (1.0)	73.2 (10.8)	48.6 (34.8)	97.3 (17.2)
Flight Video T9	2.9 (1.4)	74.9 (10.1)	41.6 (26.8)	97.9 (18.5)
Neutral Video T11	2.2 (1.1)	64.6 (8.4)	53.0 (25.2)	108.4 (21.6)
Flight Video T11	2.9 (1.6)	66.0 (9.1)	52.8 (27.5)	107.8 (22.6)

SUD = Subjective Units of Distress, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia,
PEP = Pre-Ejection Period. T2 = before diagnostic assessment (n = 79),
T3 = after individual therapeutic session 1 (n = 76), T4 = after individual therapeutic session 2 (n = 33),
T7 = first video before Cognitive Behavioral Group Therapy (CBGT) day 1 (n = 76),
T9 = second video midway CBGT day 1 (n = 63), T11 = third video after CBGT day 1 (n = 24).

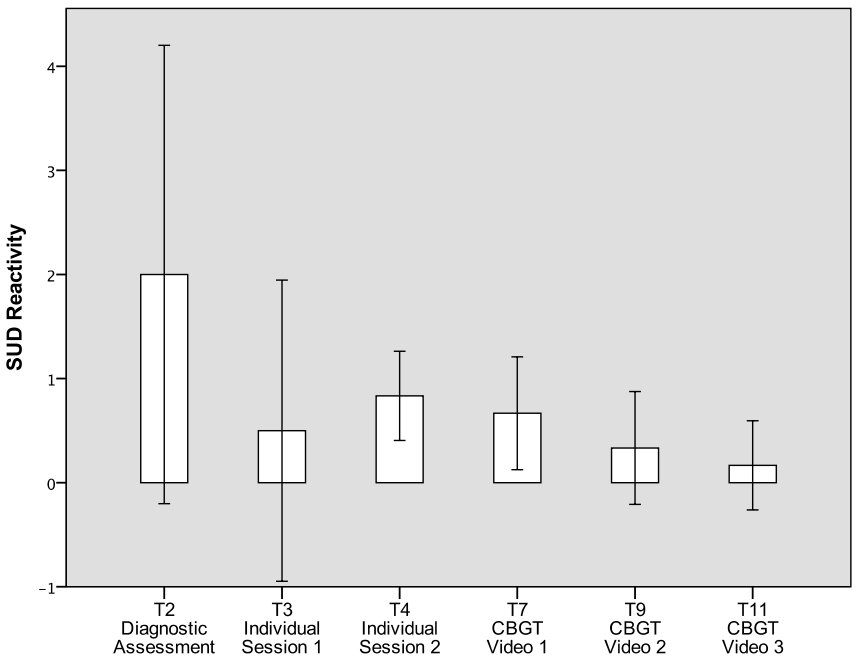

Figure 2. SUD video-reactivity before diagnostic assessment (T2 n = 79), after the first two individual therapeutic sessions (T3 n = 76, T4 n = 33) and at the first day of Cognitive Behavioral Group Therapy; T7 = first video before CBGT day 1 (n = 79), T9 = second video midway CBGT day 1 (n = 63), T11 = third video after CBGT day 1 (n = 33). Error Bars reflect 95% CI. SUD = Subjective Units of Distress, CBGT = Cognitive Behavioral Group Therapy.

Simulated flight and actual flight exposure

Fear activation

Table 3 shows absolute levels of the four variables during the baseline, pre-exposure and all eight exposure moments. MIXED ANOVA showed a significant effect of condition for SUD [$F(9, 179) = 29.0$, $p < .001$], HR [$F(9, 125.9) = 56.2$, $p < .001$], RSA [$F(9, 143.3) = 13.6$, $p < .001$] and PEP [$F(9, 86.5) = 5.3$, $p < .001$]. Post-hoc inspection showed significant fear activation for HR, RSA and PEP during each of the exposures (all $p \leq .001$). SUD reactivity showed significant fear activation for both simulator flights, taxi-out flight 1, cruise flight 1 (all $p \leq .001$) and taxi-out flight 2 ($p = .004$). As visualized in figure 3, subjective distress reactivity peaked at the first simulated flight and the beginning of both real flights but decreased from the first to the second simulated flight and during both real flights, even reaching significant ($p < .001$) lower levels than the baseline value at the

end of the second flight. In striking contrast to the flight related videos, the simulator and in-vivo exposure induced strong physiological reactivity. HR already responded to both simulated flights, but strongest responses were found during the beginning of both real flights. HR reactivity diminished during both flights, but remained 10-15 beats above baseline values throughout the entire day. Also RSA and PEP remained well below baseline during the entire day. Strongest parasympathetic and sympathetic reactivity were seen at the beginning of the first real flight.

Table 3. Mean (SD) of SUD, HR, RSA and PEP during the second day of cognitive behavioral group therapy prior to and during flight-related exposure.

	SUD	HR(bpm)	RSA(msec)	PEP(msec)
Baseline value	2.5 (1.2)	72.8 (10.0)	43.1 (26.0)	102.1 (20.2)
T12 Pre-exposure	3.2 (1.6)	78.8 (11.3)	38.9 (20.1)	96.1 (17.6)
T13 Simulator 1	4.3 (1.8)	86.9 (13.5)	32.3 (19.3)	91.5 (16.2)
T14 Simulator 2	3.0 (1.5)	86.7 (11.7)	34.5 (16.4)	91.5 (15.8)
T15 Taxi-out 1	4.0 (1.8)	98.4 (14.5)	27.9 (18.6)	87.6 (15.0)
T16 Cruise 1	3.5 (2.0)	91.1 (12.7)	33.7 (19.6)	91.4 (17.5)
T17 Taxi-in 1	2.3 (1.5)	88.2 (11.2)	32.1 (16.2)	90.8 (14.9)
T18 Taxi-out 2	3.0 (1.8)	91.5 (14.6)	30.7 (19.2)	90.0 (15.9)
T19 Cruise 2	2.5 (1.8)	87.6 (12.8)	33.7 (20.1)	91.2 (15.9)
T20 Taxi-in 2	1.6 (1.1)	84.3 (11.8)	33.7 (20.9)	92.9 (17.4)

N varies from 55 to 79. SUD = Subjective Units of Distress, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

Between-session adaptation

Between-session adaptation from the first simulator flight (T13) to the second simulator flight (T14) was significant for SUD reactivity and RSA reactivity (all $p < .001$). During the real flights, all planned contrasts [taxi-out flight 1 (T15) versus taxi-out flight 2 (T18), cruise flight 1 (T16) versus cruise flight 2 (T19), taxi-in flight 1 (T17) versus taxi-in flight 2 (T20)] showed significant between-session adaptation for SUD ($p < .001$) and HR ($p < .01$). RSA reactivity showed a trend for between-session adaptation from T15 to T18 ($p < .05$), while PEP reactivity showed a trend for between-session adaptation from T17 to T20 ($p < .05$). Solid arrows in figure 3 display the significant between-session adaptation.

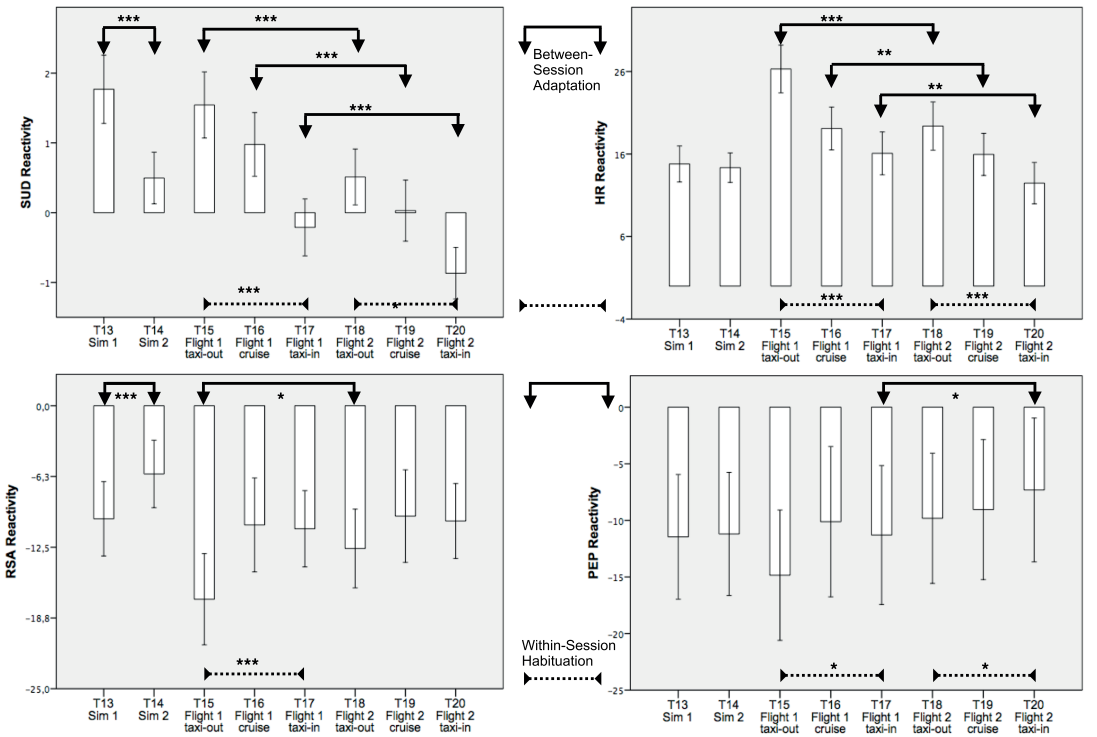

Figure 3. SUD reactivity (top left pane), HR reactivity (top right pane), RSA reactivity (bottom left pane) and PEP reactivity (bottom right pane) at both simulated flights, and at taxi-out, cruise and taxi-in during two real flights. Error Bars reflect 95% CI. SUD = Subjective Units of Distress, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period, Sim = Simulator, CI = confidence interval.
*significant at p = .05 **significant at p = .01 ***significant at p = .001

Within-session habituation

Both SUD reactivity and HR reactivity showed a significant ($p < .001$) within-session decrease during both flights (T15-T17 and T18-T20), with a trend for PEP reactivity in the same direction ($p < .05$). RSA within-session habituation reached significance only for the first flight (T15-T17, $p < .001$). Dotted arrows in figure 3 display the significant within-session habituation.

Short-term and long-term therapy outcome

Figure 4 depicts flight anxiety scores (VAFAS) at diagnostic assessment (T1), post-flight (T21), at follow-up three months after CBTG (T22), and one (T23) and three (T24) year after

treatment. Values at T1 (diagnostic assessment) were in line with the established norms for people seeking treatment for fear of flying (33, 41). Eta-square showed large effect sizes for the reduction in flight anxiety between diagnostic assessment and all later conditions, ranging from .91 at post-flight to .72 three years after therapy.

Multiple regression analyses were performed to examine whether therapy outcome could be predicted by activation of the fear network and within-session habituation and between-session adaptation of self-reported anxiety and physiological arousal. Reactivity scores for SUD, HR, RSA and PEP were all used as predictors to which the changes in reactivity within exposure sessions were added (within-session habituation), as well as the changes in reactivity across first and second exposures (between-session adaptation). Physiological variables were added in a second step to assess whether prediction improved by adding the measurements of physiological reactivity to self-report of anxiety.

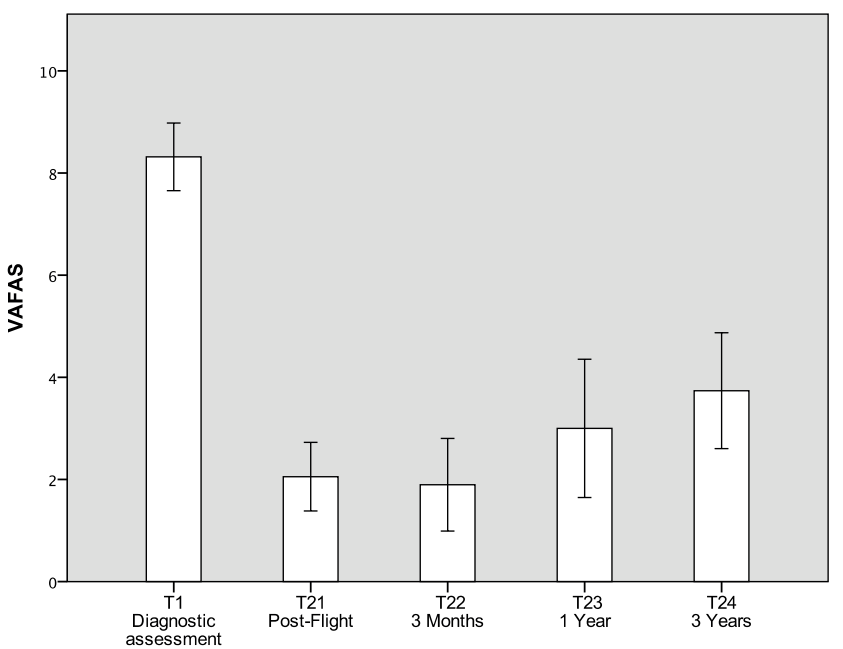

Figure 4. Bar chart of flight anxiety scores (VAFAS) at diagnostic assessment (T1 n = 79), post-flight (T21 n = 77), 3 months after treatment (T22 n = 57), and 1 (T23 n = 38) and 3 (T24 n = 67) years after treatment. Error Bars reflect 95% CI. VAFAS = Visual Analogue Flight Anxiety Scale, CI = confidence interval.

Short-term effect (flight anxiety post-flight) was predicted (R^2 = .36) by SUD reactivity during the cruise portion of the first flight (SUD at T16), in combination with HR within-session habituation over flight 1 (T15 – T17) and RSA within-session habituation over flight 2 (T18 – T20). Within-session habituation of physiological reactivity acted according to the expectation; greater HR within-session habituation over flight 1 and greater RSA within-session habituation over flight 2 were associated with less flight anxiety post-flight (Table 4). The direction of the effect for the SUD, however, was not as expected. Higher, not lower, self-reported distress reactivity during the cruise portion of the first flight was associated with higher levels of flight anxiety post-flight.

Long-term effect as defined by the VAFAS score three years after treatment was predicted (R^2 = .29) by SUD reactivity pre-exposure (T12), in combination with HR reactivity still present at the end of the second exposure flight (T20). Higher levels of SUD reactivity just before in vivo exposure corresponded with higher levels of flight anxiety three years after treatment, while a lower HR reactivity at the end of the second flight was associated with less flight anxiety three years after treatment (Table 4).

Number of flights taken in the three-year period after treatment was predicted only by SUD reactivity (R^2 = .14) during the cruise portion of the first flight (T16), as no other predictors met the inclusion criteria for the regression analysis. Again, higher, not lower, levels of self-reported distress reactivity during the cruise portion of the first flight were associated with fewer flights flown (Table 4).

Table 4. Prediction of therapy outcome by subjective and physiological reactivity and their within-session habituation and between-session adaptation (n = 67).

	Beta	SE	t	p	Zero-order correlation	R	R-Square
VAFAS Post-flight							
Step 1						.393	.154
SUD-reactivity Cruise Flight 1 (T16)	.393	.097	2.99	.004	.393		
Step 2						.600	.360
SUD-reactivity Cruise Flight 1 (T16)	.388	.086	3.13	.002	.393		
HR WSH Flight 1 (T15-T17)	-.332	.018	-2.84	.007	-.321		
RSA WSH Flight 2 (T18-T20)	.301	.522	2.58	.013	.336		
VAFAS three years after therapy							
Step 1						.455	.207
SUD-reactivity Pre-exposure (T12)	.455	.231	3.39	.001	.455		
Step 2						.534	.285
SUD-reactivity Pre-exposure (T12)	.406	.225	3.11	.003	.455		
HR-reactivity Taxi-in Flight 2 (T20)	.284	.036	2.17	.035	.353		
Number of Flights within three years							
SUD-reactivity Cruise Flight 1 (T16)	-.376	.046	-3.14	.003	-.376	.376	0.141

VAFAS = Visual Analogue Flight Anxiety Scale, SUD = Subjective Units of Distress, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, WSH = Within-Session Habituation.

DISCUSSION

In this study we followed a relatively large sample of treatment-seeking individuals with aviophobia during and after a highly standardized treatment program to overcome fear of flying. Participants in this study showed large improvements on flight anxiety measures up to three years after treatment. During exposure therapy, self-reported distress reactivity and physiological reactivity to flight-related stimuli, a flight simulator and during two real flights were assessed.

Results indicated strong fear activation for both self-report and all physiological variables during in-vivo exposure. In addition, the expected within-session habituation and between-session adaptation were evident in both subjective and physiological arousal measures. Fear activation during the flight video was only evident for self-report measures and parasympathetic activity, which is in line with reports by Bornas et al. (8, 9, 42) and Busscher et al. (4) that artificial flight stimuli elicit mixed physiological results.

Our data only partly supported the notion that alleged indicators of successful emotional processing are predictive of future flight anxiety and flight behaviour. Contrary to the expectation derived from EPT, higher levels of self-reported distress activation shortly before start of in-vivo exposure predicted higher levels of flight anxiety three years after finishing therapy. In addition, higher self-reported distress activation during the first exposure flight was associated with higher levels of flight anxiety after exposure, and less flights flown in the three years after therapy. The relationship of self-report of fear activation with negative treatment outcome seen in the current study is not in line with EPT and has recently also been reported for persons following exposure therapy for panic disorder (25), contamination fears (43) and social anxiety disorder (44), while Baker et al. (21) report that fear activation had no relationship with outcome for 44 participants with acrophobia.

The temporal pattern of diminishing physiological and subjective responses to flight (related) exposure has been reported before (7, 10, 14, 45-47). On average, at group level, almost all studies report a simultaneous habituation of both physiological reactivity and subjective reactivity in the course of exposure. Nonetheless, most support for EPT to date on within-session habituation has come from animal studies (24). The few studies with humans show inconsistent results with regard to within-session habituation and treatment outcome, and these yield no evidence for self-report of habituation as an indicator for emotional processing (7, 24, 45). Only Hayes et al. (44), in a study with

38 participants with social anxiety disorder, reports a positive relationship between decreasing SUD scores during exposure, and outcome of therapy, but only during the third (out of 5) exposure session. Here we could not substantiate these findings for flight phobics. Although on average participants had a significant diminution of SUD scores over both flights, this indication of within-session habituation did not predict therapy outcome defined either as subjective fear of flying or flying behaviour on the long-term.

The one finding in keeping with EPT was that the within-session habituation of physiological reactivity was predictive of a positive treatment outcome. Participants with greater HR habituation during the first exposure flight had lower flight anxiety scores after flight than did participants with less HR habituation. Likewise, participants with a larger increase in parasympathetic activity over the second exposure flight had less flight anxiety after the flight than did participants with a smaller increase of parasympathetic activity over flight. At first sight, this corresponds to findings by Beckham et al. (7) in 14 aviophobics (nine treatment and five control participants). The six participants who flew during the two months after exposure to a post-treatment test flight had a significantly higher HR just prior take-off, and nearly significant greater HR reduction during the test flight, than the eight participants who did not fly during the next two months. Within our group of 67 treatment completers we confirm an effect of within-session HR habituation during flight on flight-anxiety post-flight, but not on flight anxiety three years after finishing therapy or on long-term flying behaviour.

Clearly, these findings should be seen in the light of potential confounding of within-session habituation by the effects of 'general post-exposure' relief. For phobic patients, whatever their phobic disorder, subjective account will partly reveal the feeling of relief at the end of an exposure session. The decrease in SUD and physiological arousal across the two in-vivo flights could reflect this relief associated with the end of exposure as compared to imminent exposure to the phobic stimuli at the start of a flight. Participants in this study were well aware that within 45 minutes after their first flight they would board the airplane again for the second exposure flight back home. However, relief effects would be characterized by within-session habituation during the second flight only or at least mostly. Our results indicated a larger within-session habituation during the first flight than during the second flight, which does not suggest a major effect of post-exposure relief.

In the present study, despite all the indicators of adaptation of subjective distress across repeated exposures, no relationship emerged of between-session adaptation with any

treatment outcome. Adding physiological reactivity did not help; neither high levels of fear activation nor stronger between-session adaptation predicted treatment outcome. These findings add to the many studies in other domains that found contradictory results on the predictive power of between-session adaptation (21, 22, 24, 25, 44). A strong point of the current study is the use of a relatively large sample of true aviophobics in combination with self-reports of flight-anxiety and measurements of actual behaviour three years after finishing therapy. Outcome studies within the domain of fear of flying are rare. A few studies included physiological measures, however most studies lack sufficient number of participants, did not use in-vivo exposure or made use of non-clinical participants (for details see 45).

In conclusion, our results do not support most of the predictions derived from EPT. Fear activation acted partly in the opposite direction as expected, between-session adaptation of fear reactivity had no predictive value and only physiological indicators of within-session habituation had a relationship with flight anxiety directly after in vivo exposure, but were not related to long-term outcome measures. Alternatives to EPT are direly needed to explain the effectiveness of exposure therapy to change phobic behaviour. Possibly, the emphasis has been too much on affective processing at the cost of cognitive processing. Basal to exposure therapy are expectancies regarding the possibility of aversive events with negative consequences. Exposure to a feared situation without the expected aversive events actually occurring evokes extinction. Recognition of this mismatch is an information-processing activity. The active ingredient in exposure therapy might therefore be of a cognitive nature, such that changes occur in the expectancy of threat and harm (48), which then lead to reduced fear activation. As effective information processing is known to deteriorate under conditions of fear activation, this may be the source of the detrimental long-term effects we found in participants with the highest SUDs during actual flight (49, 50).

Alternatively, exposure therapy might not reduce fear activation at all but simply enhance willingness to experience and tolerate the symptoms that are induced by fear (25), which might be more challenging with severe fear reactivity. Hence, fear tolerance rather than fear reduction might have to be the primary goal of exposure therapy (22, 51). Meuret (52) reported promising results with acceptance and commitment therapy (ACT) preceding exposure. ACT may facilitate engagement in exposure exercises, thereby maximizing the mismatch effect of expected aversive events not happening, while cognitive therapy preceding exposure may reduce the expectancy of a negative outcome before exposure and thereby lessen the mismatch between initial expectancy and actual outcome (53).

Consolidation of progress could benefit from post-exposure cognitive interventions, instead of pre-exposure cognitive therapy. Recently an increasing number of publications emerged on inhibitory learning independent of fear reduction (24, 53-56). Instead of weakening of the original fear memories, these theories focus on the establishment of new memories that compete with the original fear memories (57). Exposure designed to disconfirm expectancies, exposure in multiple contexts, and the removal of safety signals during exposure could enhance treatment efficacy and prevent relapse by optimizing associative learning (43, 53, 56, 58, 59). Future studies on the effectiveness of exposure therapy focussing on optimizing conditions for exposure, in combination with the nature and timing of ancillary therapies seem warranted. Such studies would do well to measure both subjective as well as physiological aspects of fear activation. The current study confirms that these two domains provide partly independent information.

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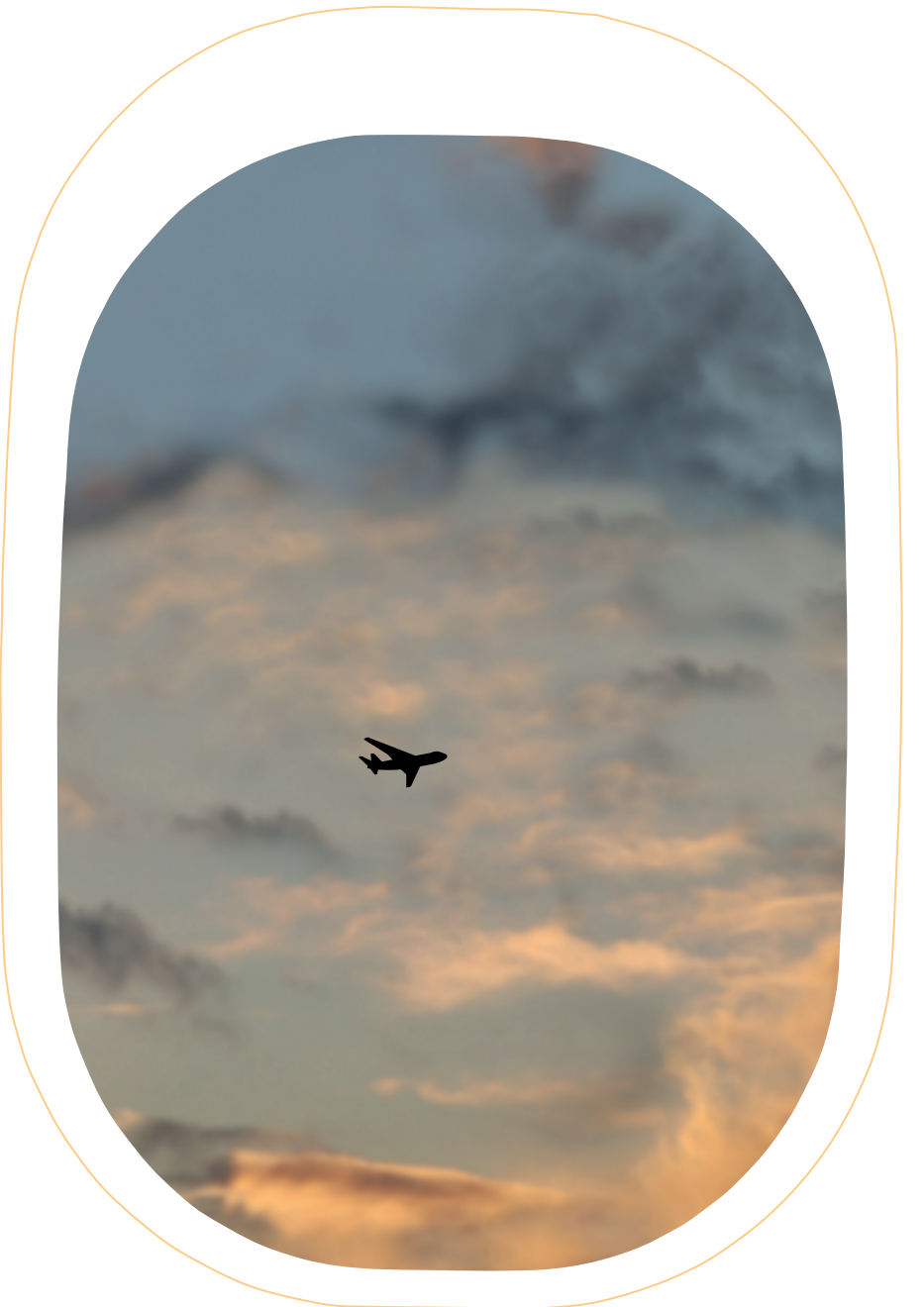

Chapter 7

Synchronous change in subjective and physiological reactivity during flight as an indicator of treatment outcome for aviophobia: a longitudinal study with 3-year follow-up

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submitted

ABSTRACT

Emotion can be seen as the organizing process that coordinates response systems to deal effectively with challenges and opportunities. Synchronous change in subjective and physiological reactivity is regarded as an indication of this organizing process. Synchrony is expected to increase with the intensity of emotional stimuli. Conversely, adaptive emotional functioning could be indicated by progressive synchrony upon increasing demands, and the magnitude of synchrony could be an indication of progress during therapy. We examined whether synchronous change in subjective and physiological reactivity over repeated exposures increased from watching a flight video through simulated flight to actual flight, and whether the magnitude of synchronous change predicted favourable short- and long-term treatment outcome within a group of 77 aviophobic participants during CBT. Results did not show a relationship between the intensity of the phobic stimuli and the magnitude of synchronous change in subjective and physiological reactivity. Moreover, synchronous change across both response systems did not predict treatment outcome. The results provide only weak support for the functionalistic view that successful treatment of anxiety disorders is indicated by synchronous change across emotional response systems. The relationship between these systems is likely to be affected by many intervening variables including higher order cognitive processes.

INTRODUCTION

Emotions enable action for survival (Frijda, 1986; Lang & McTeague, 2009). Within this functionalist view, coherence within and between biological systems (ANS, motor programs, vocalization, facial expression) facilitates coordinated responses supporting adaptive behaviour and effective communication. Coherence between biological systems is expected to increase with emotional intensity (Hollenstein & Lanteigne, 2014). Coherence can be measured as concordance or as synchrony. Whereas concordance refers to joint activation of the subsystems, synchrony refers to correlated changes in their activation over time. These temporal changes can be either in concert or in the opposite direction. Albeit intuitively appealing, evidence for concordance and synchrony is weak (Benoit Allen, Allen, Austin, Waldron, & Ollendick, 2015; Hollenstein & Lanteigne, 2014).

The tripartite model of Lang states that the emotion of fear is expressed in three loosely coupled domains: affective language, overt behaviour, and physiological reactivity (Lang, 2014; Lang & McTeague, 2009). Organized and coordinated activity between these response systems enables the individual to deal effectively with challenges (and opportunities), according to the evolutionary/functionalistic view of emotions (James, 1884; Levenson, 2014b). Emotion can be seen as the organizing process that coordinates these different systems to prepare the individual for optimal and effective response (Levenson, 2014b). When the individual is faced with increasing demands the coordinated co-activation of multiple response systems would seem even more important. Response coherence would thus be expected to increase with increasing emotional intensity. Conversely, adaptive emotional functioning could be indicated by proper and progressive response coherence upon increasing demands. If so, the magnitude of coherence could be an indication of progress during therapy. As early as 1974 Hodgson and Rachman (1974) proposed that successful treatment of anxiety disorders should be indicated by synchronous change across all three domains of the tripartite model.

A decade later several studies assessing this proposition with agoraphobic patients were published; the mixed results raised more questions than answers. Interpretation was hampered by small sample sizes and doubts about the reliability and validity of heart rate measurements, but most of all by different operationalization of concordance and synchrony. In a series of publications (Michelson, 1984; Michelson & Mavissakalian, 1985; Michelson, Mavissakalian, & Marchione, 1985) Michelson and colleagues reported that subjects showing greater HR/SUD concordance were less symptomatic than those showing less concordance. A few years later the same authors reported better outcomes,

both post-treatment and at 3-month follow-up, with participants showing synchronous change during treatment. Here, synchronous change was defined as at least one unit decrease in HR and SUD during treatment (Michelson et al., 1990). Mavissakalian (1987) followed 22 agoraphobic patients in a 12-week study involving in-vivo exposure (flooding). Both concordance and synchrony analysis revealed no relationship with outcome. Vermilyea et al. (1984) assessed 28 agoraphobic patients during a pre-, mid-, and post-treatment walk. Patients were dichotomised: synchronous patients were defined as those who showed concordant change in HR and SUD across at least two out of three walks. Treatment responders showed synchronous changes as often as desynchronous changes. A trend emerged showing treatment non-response (n=5) to have a desynchronous pattern. This trend was lost at 6-month follow-up (Craske, Sanderson, & Barlow, 1987).

A few years later Beckham et al. (1990) reported a positive relationship between HR and SUD scores five minutes after take-off and five minutes prior to landing, but not upon airport arrival, prior to take-off and directly after landing, with 14 aviophobic participants during a post-treatment flight. Synchrony was investigated over the five measurement occasions for each subject separately. A median split was done on the synchrony measures for the twelve subjects with positive correlations. Subjects with high covariation between HR and SUD showed a significantly greater improvement in their Fear of Flying score between pre- to post-flight than subjects with less covariation. Finally, no correlation between SUD and HR was found with 21 driving phobic patients during three driving sessions (Alpers, Wilhelm, & Roth, 2005), while a significant positive synchronous change between SUD fear and HR was reported with six of 10 claustrophobic patients during six exposure sessions (Alpers, 2008). However, the authors failed to relate these synchronous changes to outcome.

Over all, very few studies have reported evidence of synchrony, despite the recent growth of interest in the relationship between emotional expression and patterns of ANS activity (Hollenstein & Lanteigne, 2014; Levenson, 2014a). This might be caused by the generally low intensity and low ecological validity of the stimuli used in most laboratory studies (Hollenstein & Lanteigne, 2014). Laboratory stimuli are essentially artificial, and quite often low in intensity. Ethical constraints limit the magnitude and type of stimuli available in experimental studies. The few studies that did report coherence were all done in vivo with realistic stimuli having high intensity (Alpers, 2008; Beckham et al., 1990; Ekeberg, Kjeldsen, Greenwood, & Enger, 1990; Nesse et al., 1985). It seems that, to find synchrony and relate it to treatment outcome, more intense stimuli are needed.

Phobias might be a good starting point, as anxiety-inducing stimuli in real life generally generate intense fear responses in phobic patients.

Current Study: hypotheses

In the present study we first assessed the notion that synchronous change in subjective and physiological reactivity increases with the intensity and ecological validity of emotional stimuli. We observed a clinical sample of 77 aviophobic individuals during repeated exposure to a flight-anxiety inducing video (low intensity), to a professional flight simulator (medium intensity), and during actual flight (high intensity). Based on previous research (Busscher, van Gerwen, Spinhoven, & de Geus, 2010) we expected participants to show subjective fear responses but minimal physiological reactivity to the low intensity artificial video stimuli, resulting in minimal synchronous change in the two response systems. With the increasing ecological validity and intensity of the anxiety-inducing phobic stimuli during simulated flight and actual flight we expected increased reactivity in the two response systems paired to increased synchronous change in this reactivity over repeated exposures. Second, we assessed whether the magnitude of synchronous change predicted short- and long-term treatment outcome. Based on the assumption of Hodgson and Rachman (1974) that successful treatment of anxiety disorders should be indicated by synchronous change, we expected participants with more synchronous change in the two response systems during treatment to show lower flight anxiety at the end of treatment and three year after treatment than participants with less synchronous change during treatment, and we also expected them to have engaged in more actual flights.

MATERIAL AND METHODS

Participants

The 77 participating adults (42 women) with an average age of 40.5 (SD 11.1) in this study were individuals who applied for treatment to overcome their Fear of Flying (FOF). Some participants were referred by health care agencies, health care professionals and company health programs, although most were self-referrals. Inclusion criteria were a good understanding of the Dutch language and no flight scheduled within 5 weeks of start of treatment. Exclusion criteria were current use of cardioactive medication like β blockers, pharmacotherapeutic medication and a concurrent panic disorder of such severity, according to the treating psychotherapist, that it would seriously interfere with the treatment. Airline personnel were also excluded from this study. Written informed consent was obtained from all participants previous to the diagnostic process. The local medical ethics committee approved the research protocol.

MEASURES

Subjective Units of Distress (SUD)

The Subjective Units of Distress scale was used to examine to what extent participants were anxious at various moments. Participants had to indicate their perceived anxiety on a scale from 1 (totally relaxed) to 10 (extremely anxious) (Wolpe, 1973).

Visual Analogue Flight Anxiety Scale (VAFAS)

The single-item Visual Analogue Flight Anxiety Scale was used to examine to what extent participants were anxious about flying. The one-tailed scale ranges from 0 (no flight anxiety) to 10 (terrified or extreme flight anxiety) (Nousi, Van Gerwen, & Spinhoven, 2008).

Physiological recordings

Heart Rate (HR), Respiratory Sinus Arrhythmia (RSA) and the Pre-Ejection Period (PEP) were recorded using the VU-AMS (version 4.6, Vrije Universiteit Amsterdam, The Netherlands; www.vu-ams.nl). The VU-AMS is a lightweight ambulatory device that unobtrusively and continuously performs an electrocardiogram (ECG) and impedance cardiogram (ICG) by means of six Ag-AgCl electrodes attached to the torso region (De Geus, Willemsen, Klaver, & van Doornen, 1995; Willemsen, De Geus, Klaver, Van Doornen, & Carrol, 1996). The instrument has an event marker and an inbuilt vertical accelerometer, whose output

can be used to select movement-free periods for analysis. Automatic scoring of RSA and PEP was checked by visual inspection of the entire epoch. Details on the VU-AMS, scoring of the target variables, reliability and validity are described in detail elsewhere (Goedhart, Kupper, Willemsen, Boomsma, & de Geus, 2006; Riese, 2003). RSA is considered a measure of parasympathetic activity (Berntson et al., 1994), and PEP a measure of sympathetic activity (Sherwood et al., 1990). HR can be considered the resultant of both control systems. Fear responses are characterized by increases in HR, a decrease in RSA and shortening of the PEP.

Treatment

Participants in this study followed a highly standardized treatment program for fear of flying at the VALK foundation in The Netherlands. This institution is a joint enterprise of the Clinical Psychology Department at Leiden University with Amsterdam's Schiphol Airport and several Dutch airlines. It specializes in fear-related problems, especially fear of flying. The fear of flying program starts with a thorough diagnostic assessment, including pre-treatment phobia and flight-anxiety measurements, followed by a maximum of four individual 1-hour therapeutic sessions, covering general information on factors relevant to fear and anxiety, relaxation and breathing techniques, and coping skills. Claustrophobia, acrophobia, traumatic transportation accidents and traumatic social events were addressed where applicable. Participants started a two-day cognitive-behaviour group treatment (CBGT) five weeks after diagnostic assessment. CBGT groups consisted of a minimum of five to a maximum of eight participants, a therapist and an airline pilot. The first day of group treatment focused on psycho-education and technical information on flying. The second day focused on exposure and included two flights in a full motion cabin flight simulator normally used for flight safety training for cabin crew. The day ended with maximal in vivo exposure during guided return flights of at least one hour each on a commercial airliner. Details on therapeutic procedure have been published elsewhere (Van Gerwen, Spinhoven, & Van Dyck, 2006).

Data Collection Procedure

Before the start of the diagnostic assessment, and five weeks later before the start of the two-day CBGT, participants viewed an anxiety inducing flight-video, preceded by a neutral video, both lasting six minutes. The flight video consisted of a flight safety demonstration video of a Boeing 747 followed by some video shots of a landing Boeing 737. Subjective units of distress (SUD) were measured directly after neutral and flight video presentations. Using a visual display of the output of an inbuilt vertical accelerometer of the physiological recording device, we identified movement-free and artifact-free periods that lasted at least 5 minutes during flight-video and neutral video.

On the second day of CBGT, SUDs were collected directly after both simulator flights. Five-minute artifact-free periods within the simulated flights were selected for the physiological recording. During the two actual flights, SUDs were collected during taxi-out of the first flight and during taxi-in of the second flight. Again, movement-free and artifact-free periods lasting at least 5 minutes were selected around each of these SUD moments. All physiological reactivity scores were computed based on these 5-minute periods to ensure the temporal overlap of the subjective and physiological measurements of fear activation.

Thirty minutes after disembarking, participants filled out the VAFAS questionnaire assessing the short-term outcome of treatment regarding flight anxiety. Three years later, long-term follow-up effects of treatment were collected by email. Next to a self-report of flight anxiety (VAFAS) participants furnished the number of flights flown within the three years since end of therapy to provide a behavioural indication of treatment success.

Data analysis

Three separate conditions with increasingly realistic stimuli were used. In the first condition participants twice viewed an anxiety inducing flight video, each time preceded by a neutral video. In the second condition participants were exposed to more realistic stimuli with higher intensity during two simulated flights. The third most ecologically valid condition with highest intensity stimuli utilised two in-vivo flights. Fear reactivity to the flight video was defined as the change in the SUD variable and the three physiological variables (HR, RSA, and PEP) from the neutral and flight videos. Fear reactivity to the simulated and real flights was defined as the changes in the SUD and physiological variables during exposure, compared to a neutral baseline reflecting the entire morning (excluding flight video) of the first day of CBGT.

Pairwise t-tests and Cohen's d were calculated to assess whether there were significant changes in reactivity across repeated exposures in all three conditions. To test the first hypothesis that synchronous change between subjective and physiological reactivity increased with intensity and ecological validity of emotional stimuli, changes in the reactivity of subjective distress and of the three physiological variables across repeated exposures were computed for all three conditions. For the video stimuli, we subtracted reactivity to the second video presentation from reactivity to the first video presentation. Likewise, for the simulator we subtracted reactivity to the second simulated flight from reactivity to the first simulated flight. For the actual flight we subtracted reactivity to the end of the second flight from reactivity to the start of the first flight. This subtraction

resulted in change scores that reflect the change in subjective and physiological reactivity over repeated exposures. These change scores were used to assess the magnitude of synchronous change as the Pearson correlation coefficients between the change score for subjective distress and the change score for each of the physiological variables. Significance of the increase in these correlations with increased intensity and ecological validity was tested by the method developed by Zou (2007).

Multiple hierarchical regression analyses were used to test the second hypothesis that a higher amount of synchronous change is associated with better treatment outcome. Separate analyses were performed for video-, simulator- and flight-exposure. Predictor variables were the SUD, HR, RSA and PEP changes from first- to second- exposure. The products of the SUD change scores with the physiological change scores were added to the regression models in the second step of the regression analyses. Significance of a two-way interaction in this second step of the regression model would be an indication that synchronous change was related to treatment outcome (Benoit Allen et al., 2015). For example, a significant interaction between changes in SUD and changes in HR would indicate that synchrony between these two components was associated with treatment outcome. Short-term outcome was operationalized as the flight anxiety score taken directly after the second exposure flight. Long-term outcome was operationalized as the flight anxiety score three years after treatment, and number of flights taken in this three-year period. To compensate for individual baseline differences in the flight anxiety outcome variables these anxiety scores were regressed on the flight anxiety score taken during diagnostic assessment. After analyses of the relationship between age and gender with all variables of interest we concluded that it was not necessary to control for both variables in further analyses. Throughout all regression analyses we first computed saved standardized residuals by regression of second exposure reactivity scores on first exposure reactivity scores, and subsequently used them as independent variables in the final regression analyses. This way it was not necessary to control for baseline values in an additional first step in the hierarchical regression analysis; this procedure reduced the number of predictor variables while reaching similar results.

The security checks at the airports turned out to be a major challenge for the physiological measurements. The attached electrodes of the ambulatory measurement device required a physical patting down of all participants. Consequently, data on one or more physiological variables during flight were lost for 15 participants. Data of two participants were lost due to equipment failure during flight. One flight was cancelled due to adverse weather, resulting in the loss of flight data of two participants. All available data were

used for analysis without excluding participants, as data loss was completely random. Missing data were not replaced or substituted. RSA and Number of Flights Flown within three years of end of therapy were log (Ln) transformed to obtain normal distributions.

RESULTS

Table 1 shows subjective and physiological reactivity across repeated exposures in the three conditions. As expected, participants showed marked subjective fear responses and minimal physiological reactivity to the low intensity artificial video stimuli. Physiological reactivity increased progressively from video to simulator to real flight exposure, but less so for the second than the first exposure, resulting in marked changes across repeated measurements in the flight condition. Subjective reactivity showed progressively larger changes across repeated measurements from video to simulator to real flight exposure. Pearson correlation coefficients were computed as an indication of synchrony in the changes in subjective and physiological reactivity. Only weak evidence for synchrony was found and, contrary to our first hypothesis, in the most intense and ecologically valid condition none of these correlations proved to be significant[1] (table 2).

Multiple hierarchical regression analyses were performed to test the second hypothesis that participants with more synchronous change in the two response systems during treatment would show better short-term and long-term treatment outcomes than would participants with less synchronous change during treatment. Changes in subjective (SUD) and physiological (HR, RSA, PEP) reactivity were added in the first step of the regression analyses. In a second step all two-way interactions (SUD/HR, SUD/RSA and SUD/PEP) were added. This was the critical test of our second hypothesis, where significance of a two-way interaction would be an indication that more synchronous change would predict better treatment outcome. Contrary to this hypothesis, the results revealed no significant interaction effect in any condition for none of the three paired variables (SUD/HR, SUD/RSA and SUD/PEP).

[1] Simple change scores were used to facilitate interpretation of changes in reactivity across repeated exposures. For consistency, Pearson correlation coefficients were computed based on these simple change scores. We also reran the analyses computing saved standardized residuals by regressing second exposure reactivity scores on first exposure reactivity scores, and subsequently used them in further analyses. This led to highly similar results.

Table 1. Reactivity of SUD, HR, RSA and PEP to First and Second exposure to the phobic stimuli in the three conditions and the Change in reactivity across repeated exposure.

Condition	First	Second	Change	t	p	Cohen's d
Video						
SUD	1.36 (1.6)	.87 (1.3)	.49 (1.4)	2.99	.004	.34
HR	-.179 (3.2)	.104 (2.5)	-.28 (3.6)	-.67	.503	.10
RSA (ms)	-2.82 (15.3)	-.12 (10.0)	-2.70 (16.7)	-1.28	.204	.19
PEP (ms)	.32 (3.3)	.24 (3.7)	.081 (4.8)	.145	.885	.02
Simulator						
SUD	1.77 (1.8)	.38 (1.3)	1.39 (1.4)	7.025	< .001	.89
HR	14.4 (8.9)	14.3 (7.2)	.27 (6.1)	.358	.722	.01
RSA (ms)	-11.4 (18.1)	-9.57 (19.1)	-1.83 (9.5)	-3.25	.002	.28
PEP (ms)	-11.5 (21.6)	-11.2 (22.6)	-.29 (5.5)	-.434	.665	.02
Flight						
SUD	1.57 (2.0)	-.80 (1.6)	2.36 (1.8)	10.7	< .001	1.31
HR	25.7 (11.2)	12.7 (9.6)	13.0 (8.1)	11.7	< .001	1.25
RSA (ms)	-18.3 (17.5)	-13.0 (16.6)	-5.25 (12.9)	-3.14	.003	.40
PEP (ms)	-13.2 (21.6)	-8.84 (22.7)	-4.38 (8.85)	-3.6	.001	.20

SUD = Subjective Units of Distress, HR = Heart Rate,
RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

Table 2. Correlation coefficients of changes in subjective reactivity with changes in physiological reactivity across repeated exposure in the three conditions.

	SUD with	HR	RSA	PEP
Condition				
Video		.303 **	.031	-.166
Simulator		.189	-.301 *	-.053
Flight		-.035	-.074	.098

* significant at .05 ** significant at .001.

Main effects for changes in SUD and HR emerged during the flight exposure, and a main effect for changes in HR emerged during the simulator exposure, both for short-term outcome. Participants with less diminution in HR over simulated flights reported less decrease in flight anxiety from beginning to end of therapy than participants with more diminution of HR over the simulated flights. Participants who reported less decrease in distress over real flights reported less decrease in flight anxiety from beginning to end of therapy than participants who reported a larger decrease in distress over real flights, and participants with less diminution in HR over real flights reported less decrease in flight anxiety from beginning to end of therapy than participants with more diminution of HR over both real flights (results partly published in Busscher, Spinhoven, van Gerwen,

Table 3. Regression analyses of short-term treatment outcome on changes over flights in subjective distress (SUD) and changes over flights in physiological measures (HR, RSA and PEP) and their interaction.

	VAFAS Short-term				
	B	SE	t	p	Zero-order correlations
Step 1					
Constant	.10	.144	.070	.944	-
SUD changes	.423	.157	2.699	.011	.303
HR changes	.476	.169	2.813	.008	.309
RSA changes	.252	.153	1.646	.108	-.035
PEP changes	.059	.158	.375	.710	-.074
Step 2					
Constant	-.074	.158	-.469	.642	-
SUD changes	.571	.220	2.597	.014	.303
HR changes	.422	.171	2.460	.019	.309
RSA changes	.252	.163	1.546	.132	-.035
PEP changes	-.006	.170	-.033	.974	-.074
Interaction SUD-HR	-.361	.203	-1.777	.085	-.162
Interaction SUD-RSA	-.083	.173	-.482	.633	-.029
Interaction SUD-PEP	004	.213	.017	.987	-.164

VAFAS = Visual Analogue Flight Anxiety, SUD = Subjective Units of Distress, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

& de Geus, 2013). Table 3 illustrates the regression model for the flight condition with the short-term effect on flight anxiety as the dependent treatment outcome variable. Detailed results of all outcomes in all conditions (video-exposure, simulator-exposure and flight-exposure) are provided in the supplemental materials section.

DISCUSSION

For more than 130 years (James, 1884) emotion has been conceptualised as the organising entity that coordinates response systems to aid survival. Response coherence is expected to mirror this process, even more so during demanding circumstances (Hollenstein & Lanteigne, 2014). Evidence for concordance in the reactivity of the response systems and synchronous change in their reactivity over time has been sparse (Alpers, 2008; Beckham et al., 1990; Ekeberg et al., 1990; Nesse et al., 1985). This was hypothesized to have been caused by the generally low intensity of the stimuli used in the published research (Hollenstein & Lanteigne, 2014; Levenson, 2014a). Therefore, in the present study we followed highly aviophobic participants who were exposed to increasingly realistic and ecologically valid stimuli, including two actual flights. Participants showed marked subjective and physiological reactivity, and marked changes across repeated exposures, especially in the actual flight condition. Nevertheless, at group level, these intense and ecologically very valid stimuli did not evoke synchronous change in self-reported and physiological reactivity. So far, little proof has been provided that synchronous change is coupled to intensity of stimuli and emotional functioning (Hollenstein & Lanteigne, 2014; Levenson, 2014a). Individual reactivity in each of the two response systems was coupled to treatment outcome. However, synchronous change in the two systems was not indicative of short-term and long-term treatment results. Results in the present study are therefore not in line with the assumption of Hodgson and Rachman (1974) that successful treatment of anxiety disorders should be indicated by synchronous change.

Results from empirical studies often add complexity to an attractive theoretical perspective. Of course, the model could be wrong. It is conceivable that research on coherence is subject to the file-drawer phenomenon and that many null findings have not been published. Nevertheless, null findings are not refutations. Maybe the coordinating role of emotion is not at all mirrored by response coherence. On the other hand, other processes might conceal this relationship. Emotion regulation is a complex process that includes conscious and unconscious physiological, behavioural and cognitive processes that modulate emotions to respond appropriately to environmental demands (Aldao,

Nolen-Hoeksema, & Schweizer, 2010; Gross, 2001; Thompson, 1991; Thompson, 1994). Cognitive coping strategies like self-blame, rumination, catastrophizing and avoidance play a prominent role within the anxiety pathologies (Garnefski et al., 2002; Martin & Dahlen, 2005). For example, cognitive avoidance, the conscious suppression of unwanted thoughts, could counterproductively lead to increased accessibility of the suppressed thoughts and hence result in hypersensitivity to anxiety-related thoughts and symptoms (Wegner & Zanakos, 1994; Wenzlaff & Wegner, 2000). Cognitive coping strategies could mediate the relationship between self-report of anxiety and the psychophysiological components of anxiety. We judge and feel emotions about our emotions. Perceiving an emotion as unacceptable, problematic, or aversive, instead of normal, can influence the way a person regulates the emotional state itself (Couyoumdjian et al., 2016; Schaefer, Larson, Davidson, & Coan, 2014). Couyoumdjian et al. (2016) report preliminary evidence that a reduction in negative self-evaluation contributed to a decrease of autonomic arousal in reaction to a phobic stimulus. Sixteen animal phobic participants, who received a short cognitive treatment to reduce dysfunctional thoughts about the self, showed a reduced physiological arousal (decreased HR and increased HRV) but no change in subjective symptoms during and shortly after exposure to an individualized phobic video clip. The seventeen phobic control participants who did not receive treatment showed no change in physiological and subjective symptoms of anxiety during and after phobic exposure.

Phobic provocation is an intensely fearful experience. A conflict between uncontrollable, automatic phobic reaction and the recognition that the phobic fear response is irrational and even embarrassing may lead to an increased attempt at emotion regulation, in an effort to suppress or control the fear reaction (Schaefer et al., 2014). The effect of cognitive behavioural therapy might partly be explained by additional cognitive regulation strategies being brought online to dampen automatic and coherent responses. The time course of emotion subsystems may vary greatly (Hollenstein & Lanteigne, 2014; Levenson, 2014b), and may vary even more owing to this additional cognitive regulation. Cross-correlation concordance analyses with short time-windows (-10 seconds to + 10 seconds) have been used to compensate for the different temporal characteristics of response systems (Butler, Gross, & Barnard, 2014; Dan-Glauser & Gross, 2013; Mauss, Levenson, McCarter, Wilhelm, & Gross, 2005; Sze, Gyurak, Yuan, & Levenson, 2010). However, as far as we know no lagged cross-correlation analyses on synchronous change have been published. In the present study we used 5-minute time windows around each of the SUD moments for the physiological measures during the flight condition, thereby effectively compensating for short-term temporal deviations.

Strengths, limitations and future directions

As in many studies on coherence, participants retrospectively reported SUDs immediately after the video presentations and both simulated flights, whereas ANS responses were acquired during the phobic induction itself. Ideally, coherence should be examined with simultaneous acquisition of ANS and experiential variables (Hollenstein & Lanteigne, 2014; Levenson, 2014b). During the actual flight physiological- and SUD-measurements had a perfect temporal overlap, preventing retrospective memory biases. The present study used a straightforward definition of synchronous change combined with an unambiguous operationalization of fear intensity. Individual subjective and physiological baseline differences were effectively compensated (Hollenstein & Lanteigne, 2014; Levenson, 2014b). Another positive point was the use of two entirely different clinically relevant long-term outcome measures: a behavioural measure indicating flight behaviour and a self-report measure indicating flight anxiety. However, subjective reactivity during the phobic inductions was assessed by one single questionnaire only. Furthermore, the behavioural component of the tripartite model was not tested.

Fear is invoked in situations where action is required (van Duinen, Schruers, & Griez, 2010). A primary function is to redirect energy resources to prepare the body for flight or fight. This surplus of available energy is of no use once one is inside an airplane because overt behaviour is severely restricted in this situation. The discrepancy between action-readiness and the inability to execute physical motion is very clear in this example, but actually applies to all the research on concordance. Only Vermilyea et al. (1984) had agoraphobic patients actually walk during assessment, and reported treatment responders to have synchronous changes as often as desynchronous changes. The influence of suppression of overt behaviour on synchronous changes in subjective reports of distress and physiological measures of arousal warrants further study.

Another positive point of the present study is the use of multiple measures of ANS reactivity as recommended by Hollenstein and Lanteigne (2014). HR is the most commonly used physiological measure in coherence research (Levenson, 2014b). HR is a sensitive measure that captures phobic fear intensity at both extremes of the fear continuum (Aue, Hoeppli, & Piguet, 2012; Kreibig, 2010; Wilhelm & Grossman, 2010). Furthermore, it has high face validity. However, HR changes are foremost caused by bodily needs to restore homeostasis. Emotion is just one of many influences on the ANS. The heart is dually innervated: at rest, HR is under parasympathetic restraint slowing the intrinsic pacemaker cells from approximately 100 beats per minute to a mere 70 beats per minute. Increased sympathetic activity, but also reduced parasympathetic activity, will

increase HR. For example, Hu, Lamers, de Geus, and Penninx (2016) report in a large group of people with depressive and anxiety disorders that increased ANS stress reactivity to an ecologically valid stressor was probably caused by vagal withdrawal. HR alone does not indicate which branch of the autonomic system influences the heart. RSA and PEP, as also used in the present study, are more informative. Alternative non-intrusive reliable and sensitive measures to capture ANS activity in an ambulatory setting are few. For example, electrodermal activity is susceptible to movement artifacts, pupil dilation measurement is hardly feasible under naturalistic conditions, and endocrine measures via saliva collection may alter behaviour (Alpers, W., 2009; Kreibig, 2010; Wilhelm & Grossman, 2010). Nevertheless, future research could benefit from moving beyond cardiac measures (Levenson, 2014a).

Response coherence has been difficult to capture, and poses a number of methodological and data-analytic challenges (Bulteel et al., 2014). Most research on coherence used a between-subjects rather than a within-subjects approach (Levenson, 2014b). To find synchronous change in reactivity across response systems, studies need to assess and correlate this reactivity within the same individual (Hollenstein & Lanteigne, 2014; Levenson, 2014b). Here we used such a within-subject design, following a previous study by Benoit Allen et al. (2015), to test the hypothesis that increased synchronous change is coupled with better treatment results. The possible delayed effect of emotion regulation on the tripartite components requires new longitudinal analytic approaches to statistically model the process of synchronous change of multiple response systems with different temporal characteristics.

Clinical implications

The aim of cognitive behavioural therapies is to "*help individuals to optimize their adaptation to circumstances that arise in their lives*" (Mennin, Ellard, Fresco, & Gross, 2013, p. 236) by fostering flexibility and promoting behavioural adaptation. It has been thought that the magnitude of coherence could be an indication of progress during therapy; however, the relationship between domains is not straightforward and is possibly affected by many intervening processes and variables. Higher order cognitive processes seem to intervene with the supposititious temporal associations between responses (Mauss et al., 2005; Schaefer et al., 2014). If an effect of cognitive therapy is a reduction of automatic and coherent responses between domains, then this might lead to a lagged or reduced physiological fear response (Schaefer et al., 2014). Blunted physiological fear responses might diminish effectiveness of (in-vivo) exposure therapy, as according to the emotional processing theory (EPT) (Foa & Kozak, 1986), fear activation is a prerequisite

for fear-extinction. Cognitive interventions, aimed at alleviating fear or at promoting regulating strategies that dampen automatic and coherent responses, might better be postponed to after the exposure component of the treatment (Busscher, Spinhoven, & de Geus, 2015; Craske, Treanor, Conway, Zbozinek, & Vervliet, 2014). Furthermore, treatment programs would do best not to focus too much on concordant changes in self-reported and physiological indicators of arousal.

CONCLUSION

Results in the present study did not show a relationship between the intensity of the phobic stimuli and the magnitude of synchronous change in subjective and physiological reactivity. Furthermore, even with exposure to ecologically valid stimuli of high phobic intensity, we did not find evidence that a higher magnitude of synchronous change is coupled to a more favourable treatment outcome. For the time being, the functionalistic view that successful treatment of anxiety disorders is indicated by synchronous change between the tripartite domains remains a hypothesis with high face validity, but a very poor empirical basis.

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7

SUPPLEMENTAL MATERIAL

Synchronous change in subjective and physiological reactivity during flight as an indicator of treatment outcome for aviophobia: a longitudinal study with 3-year follow-up

Bert Busscher, Philip Spinhoven, Eco J. C. de Geus

SUPPLEMENTAL MATERIAL

Multiple hierarchical regression analyses were used to test the hypothesis that a higher amount of synchronous change is associated with better treatment outcome. Separate analyses were performed for video-, simulator- and flight-exposure. Predictor variables were the SUD, HR, RSA and PEP changes from first- to second- exposure. The products of the SUD change scores with the physiological change scores were added to the regression models in the second step of the regression analyses. Significance of a two-way interaction in this second step of the regression model would be an indication that synchronous change was related to treatment outcome. For example, a significant interaction between changes in SUD and changes in HR would indicate that synchrony between these two components was associated with treatment outcome. Short-term outcome was operationalized as the flight anxiety score taken directly after the second exposure flight. Long-term outcome was operationalized as the flight anxiety score three years after treatment, and number of flights taken in this three-year period. To compensate for individual baseline differences in the flight anxiety outcome variables these anxiety scores were regressed on the flight anxiety score taken during diagnostic assessment. Throughout all regression analyses we first computed saved standardized residuals by regression of second exposure reactivity scores on first exposure reactivity scores, and subsequently used them as independent variables in the final regression analyses. This way it was not necessary to control for baseline values in an additional first step in the hierarchical regression analysis; this procedure reduced the number of predictor variables while reaching similar results.

Contrary to this hypothesis, the results revealed no significant interaction effect in any condition for none of the three paired variables (SUD/HR, SUD/RSA and SUD/PEP). Main effects for changes in SUD and HR emerged during the flight exposure, and a main effect for changes in HR emerged during the simulator exposure, both for short-term outcome. Participants with less diminution in HR over simulated flights reported less decrease in flight anxiety from beginning to end of therapy than participants with more diminution of HR over the simulated flights. Participants who reported less decrease in distress over real flights reported less decrease in flight anxiety from beginning to end of therapy than participants who reported a larger decrease in distress over real flights, and participants with less diminution in HR over real flights reported less decrease in flight anxiety from beginning to end of therapy than participants with more diminution of HR over both real flights.

Table 1a. Regression analyses of short-term treatment outcome (flight anxiety) on changes over video-exposure in subjective distress (SUD) and changes over video-exposure in physiological measures (HR, RSA and PEP) and their interaction.

	VAFAS Short-term				
	B	SE	t	p	Zero-order correlations
Step 1					
Constant	-.052	.123	-.421	.676	-
SUD changes	-.045	.147	-.307	.760	.095
HR changes	.163	.143	1.143	.258	.114
RSA changes	.214	.152	1.404	.166	.160
PEP changes	-.055	.131	-.421	.675	-.085
Step 2					
Constant	-.133	.143	-.931	.356	-
SUD changes	-.036	.147	-.242	.810	.095
HR changes	.161	.144	1.123	.267	.114
RSA changes	.184	.154	1.196	.237	.160
PEP changes	-.053	.142	-.374	.710	-.085
Interaction SUD-HR	-.140	.132	-1.063	.292	-.167
Interaction SUD-RSA	.199	.139	1.429	.159	.195
Interaction SUD-PEP	-.175	.154	-1.135	.261	-.028

VAFAS = Visual Analogue Flight Anxiety, SUD = Subjective Units of Distress,
HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

Table 1b. Regression analyses of short-term treatment outcome (flight anxiety) on changes over simulator-exposure in subjective distress (SUD) and changes over simulator-exposure in physiological measures (HR, RSA and PEP) and their interaction.

	VAFAS Short-term				
	B	SE	t	p	Zero-order correlations
Step 1					
Constant	-.137	.135	-1.1017	.318	-
SUD changes	-.176	.131	-1.345	.189	-.005
HR changes	.745	.149	4.985	< .001	.645
RSA changes	.029	.150	.194	.847	-.118
PEP changes	.158	.109	1.443	.160	.107
Step 2					
Constant	-.169	.164	-1.035	.311	-
SUD changes	-.229	.186	-1.235	.228	-.005
HR changes	.705	.166	4.245	< .001	.645
RSA changes	-.027	.172	-.156	.877	-.118
PEP changes	.175	.126	1.388	.177	.107
Interaction SUD-HR	-.059	.179	-.328	.746	-.101
Interaction SUD-RSA	-.139	.146	-.957	.348	-.124
Interaction SUD-PEP	-.028	.177	-.158	.876	-.126

VAFAS = Visual Analogue Flight Anxiety, SUD = Subjective Units of Distress,
HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

Table 1c. Regression analyses of short-term treatment outcome (flight anxiety) on changes over flights in subjective distress (SUD) and changes over flights in physiological measures (HR, RSA and PEP) and their interaction.

	VAFAS Short-term				
	B	SE	t	p	Zero-order correlations
Step 1					
Constant	.10	.144	.070	.944	-
SUD changes	.423	.157	2.699	.011	.303
HR changes	.476	.169	2.813	.008	.309
RSA changes	.252	.153	1.646	.108	-.035
PEP changes	.059	.158	.375	.710	-.074
Step 2					
Constant	-.074	.158	-.469	.642	-
SUD changes	.571	.220	2.597	.014	.303
HR changes	.422	.171	2.460	.019	.309
RSA changes	.252	.163	1.546	.132	-.035
PEP changes	-.006	.170	-.033	.974	-.074
Interaction SUD-HR	-.361	.203	-1.777	.085	-.162
Interaction SUD-RSA	-.083	.173	-.482	.633	-.029
Interaction SUD-PEP	.004	.213	.017	.987	-.164

VAFAS = Visual Analogue Flight Anxiety, SUD = Subjective Units of Distress, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

Table 2a. Regression analyses of long-term treatment outcome (flight anxiety) on changes over video-exposure in subjective distress (SUD) and changes over video-exposure in physiological measures (HR, RSA and PEP) and their interaction.

	VAFAS Long-term				
	B	SE	t	p	Zero-order correlations
Step 1					
Constant	-.083	.121	-.685	.496	-
SUD changes	.020	.133	.147	.884	.039
HR changes	.043	.141	.303	.763	.092
RSA changes	-.019	.158	-.119	.906	-.060
PEP changes	-.077	.123	-.628	.533	-.108
Step 2					
Constant	-.122	.134	-.912	.366	-
SUD changes	-.048	.146	-.330	.742	.039
HR changes	.029	.152	.192	.848	.092
RSA changes	-.117	.167	-.701	.486	-.060
PEP changes	-.084	.129	-.648	.520	-.108
Interaction SUD-HR	-.089	.179	-.500	.619	.040
Interaction SUD-RSA	-.299	.176	-1.695	.096	-.200
Interaction SUD-PEP	-.046	.132	-.350	.728	-.098

VAFAS = Visual Analogue Flight Anxiety, SUD = Subjective Units of Distress, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

Table 2b. Regression analyses of long-term treatment outcome (flight anxiety) on changes over simulator-exposure in subjective distress (SUD) and changes over simulator-exposure in physiological measures (HR, RSA and PEP) and their interaction.

	VAFAS Long-term				
	B	SE	t	p	Zero-order correlations
Step 1					
Constant	.129	.166	.775	.445	-
SUD changes	.285	.212	1.346	.189	.222
HR changes	-.445	.196	-2.276	.031	-.240
RSA changes	-.129	.226	-.571	.572	.041
PEP changes	-.335	.149	-2.255	.032	-.275
Step 2					
Constant	.034	.197	.171	.866	-
SUD changes	.043	.329	.129	.898	.222
HR changes	-.467	.302	-1.543	.136	-.240
RSA changes	-.209	.310	-.673	.507	.041
PEP changes	-.283	.172	-1.648	.112	-.275
Interaction SUD-HR	.032	.521	.062	.951	.331
Interaction SUD-RSA	-.276	.520	-.531	.600	-.274
Interaction SUD-PEP	.154	.340	.452	.655	-.100

VAFAS = Visual Analogue Flight Anxiety, SUD = Subjective Units of Distress, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

Table 2c. Regression analyses of long-term treatment outcome (flight anxiety) on changes over flights in subjective distress (SUD) and changes over flights in physiological measures (HR, RSA and PEP) and their interaction.

	VAFAS Long-term				
	B	SE	t	p	Zero-order correlations
Step 1					
Constant	-.039	.163	-.237	.814	-
SUD changes	.024	.152	.158	.876	.036
HR changes	.068	.185	.369	.715	.119
RSA changes	.003	.193	.017	.987	-.025
PEP changes	-.122	.177	-.691	.495	-.164
Step 2					
Constant	-.089	.174	-.509	.615	-
SUD changes	.098	.201	.487	.631	.036
HR changes	.032	.193	.164	.871	.119
RSA changes	-.008	.243	-.033	.974	-.025
PEP changes	-.175	.189	-.928	.362	-.164
Interaction SUD-HR	-.292	.254	-1.149	.261	-.105
Interaction SUD-RSA	-.063	.241	-.263	.795	-.009
Interaction SUD-PEP	-.148	.167	-.884	.385	-.076

VAFAS = Visual Analogue Flight Anxiety, SUD = Subjective Units of Distress,
HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

Table 3a. Regression analyses of long-term treatment outcome (number of flights taken within three years after treatment) on changes over video-exposure in subjective distress (SUD) and changes over video-exposure in physiological measures (HR, RSA and PEP) and their interaction.

	Number of Flights				
	B	SE	t	p	Zero-order correlations
Step 1					
Constant	.052	.128	.408	.685	-
SUD changes	-.146	.151	-.966	.338	-.256
HR changes	-.097	.154	-.628	.533	-.119
RSA changes	-.214	.155	-1.384	.172	-.244
PEP changes	.008	.126	.061	.952	.056
Step 2					
Constant	.079	.148	.533	.597	-
SUD changes	-.133	.154	-.864	.392	-.256
HR changes	-.143	.162	-.887	.379	-.119
RSA changes	-.200	.158	-1.266	.212	-.244
PEP changes	.044	.134	.328	.744	.056
Interaction SUD-HR	-.132	.155	-.857	.396	-.124
Interaction SUD-RSA	.057	.139	.411	.683	.078
Interaction SUD-PEP	.027	.145	.189	.851	.068

SUD = Subjective Units of Distress, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period.

Table 3b. Regression analyses of long-term treatment outcome (number of flights taken within three years after treatment) on changes over simulator-exposure in subjective distress (SUD) and changes over simulator-exposure in physiological measures (HR, RSA and PEP) and their interaction

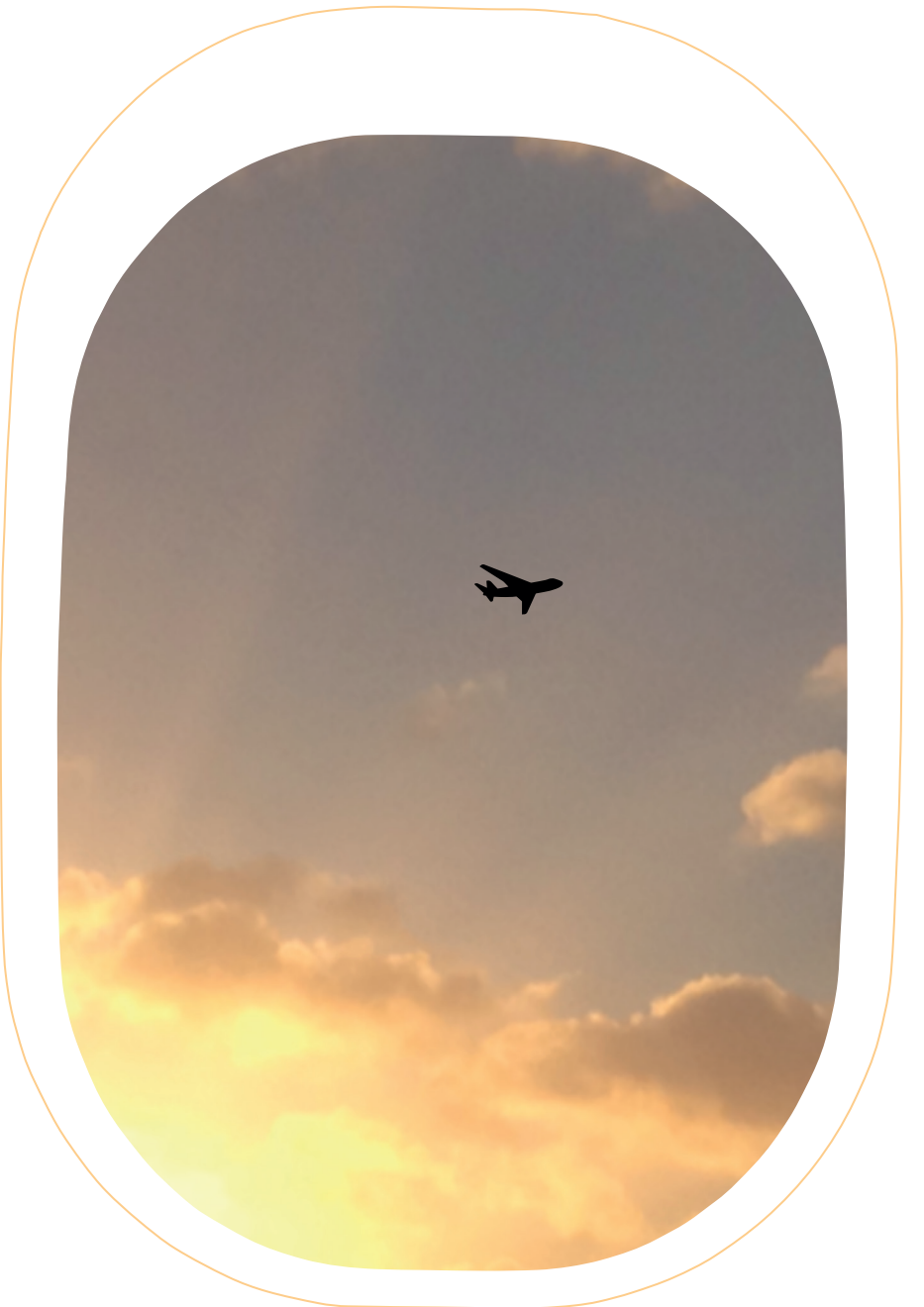
	Number of Flights				
	B	SE	t	p	Zero-order correlations
Step 1					
Constant	.181	.202	.900	.377	-
SUD changes	.053	.204	.259	.798	-.001
HR changes	.052	.201	.258	.798	.062
RSA changes	.187	.210	.892	.380	.093
PEP changes	-.234	.159	-1.471	.153	-.255
Step 2					
Constant	.250	.257	.973	.341	-
SUD changes	.037	.286	.129	.899	-.001
HR changes	.028	.220	.126	.901	.062
RSA changes	.256	.253	1.010	.323	.093
PEP changes	-.298	.191	-1.565	.131	-.255
Interaction SUD-HR	-.086	.297	-.289	.775	.105
Interaction SUD-RSA	-.004	.234	-.018	.985	-.118
Interaction SUD-PEP	-.270	.287	-.940	.357	-.099

SUD = Subjective Units of Distress, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period

Table 3c. Regression analyses of long-term treatment outcome (number of flights taken within three years after treatment) on changes over flights in subjective distress (SUD) and changes over flights in physiological measures (HR, RSA and PEP) and their interaction

	Number of Flights				
	B	SE	t	p	Zero-order correlations
Step 1					
Constant	-.091	.204	-.444	.661	-
SUD changes	-.022	.195	-.113	.911	-.018
HR changes	-.252	.242	-1.042	.306	-.076
RSA changes	-.136	.230	-.592	.559	-.044
PEP changes	-.283	.211	-1.340	.191	-.191
Step 2					
Constant	-.071	.208	-.342	.735	-
SUD changes	-.238	.265	-.900	.736	-.018
HR changes	-.217	.245	-.885	.384	-.076
RSA changes	-.179	.240	-.746	.462	-.044
PEP changes	-.253	.215	-1.181	.248	-.191
Interaction SUD-HR	-.547	.402	-1.362	.185	-.087
Interaction SUD-RSA	-.126	.237	-.532	.599	-.104
Interaction SUD-PEP	-.476	.264	-1.799	.084	-.168

SUD = Subjective Units of Distress, HR = Heart Rate, RSA = Respiratory Sinus Arrhythmia, PEP = Pre-Ejection Period



Chapter 8

Summary and general discussion

SUMMARY AND GENERAL DISCUSSION

The main aim of the empirical studies in this thesis was to increase the available knowledge on individual differences in subjective and physiological reactivity to flight (related) stimuli in people with serious fear of flying. A second objective was to elucidate the added value of psychophysiological measures for diagnosis of aviophobia and for prognosis of treatment outcome. This final chapter summarizes and discusses the findings of the empirical studies.

SUMMARY OF RESULTS

Chapter 2

The question addressed in chapter two was whether aviophobics have an exaggerated physiological arousal that leads to an exaggerated subjective arousal during exposure to anxiety-related stimuli, or whether the exaggerated subjective arousal is caused by misinterpretation of normal bodily sensations as is often the case with individuals high on anxiety sensitivity. We found that aviophobic participants reported significantly higher levels of subjective fear than did control participants when exposed to a video with flight-related stimuli. In contrast, on average the three physiological variables (heart rate (HR), respiratory sinus arrhythmia (RSA), and pre-ejection period (PEP)) did not differ between the two groups, although the phobic participants showed a much stronger variation in cardiac parasympathetic reactivity. Anxiety sensitivity did not moderate the relationship between self-reported anxiety and recorded physiological arousal. These results emphasize the heterogeneous nature of aviophobia, with large inter-individual differences in reactivity to stimuli of low ecological validity (Bornas et al. 2004, 2005, 2006).

Chapter 3

Graded in-vivo exposure with aviophobics is challenging, and especially the last step. To board, or not to board, that is the question. A little boarding does not exist. Cognitive interventions prior to in-vivo exposure increase confidence in the ability to handle the last step. Another helpful tool to ease anxiety associated with the last step is graded exposure by means of Virtual Reality. This technique enables cost-effective often-repeated exposures, as well as exposure graded according to a fear hierarchy (Powers and Emmelkamp 2008). Therapists monitor the anxiety levels, and patients accordingly progress through their fear hierarchy. Basal to this approach are reliable and valid

indicators of anxiety and arousal, preferably with a baseline measurement in a neutral virtual world. Chapter 3 describes two studies on baseline measurements in Virtual Reality. In the first study both phobic and non-phobic participants showed higher heart rates during exposure in a neutral virtual world than in a virtual world with phobic stressors, and in the recovery phase after the VR exposure. This led to the conclusion that the previously used neutral world (Schuemie 2003) was probably not truly neutral after all. In the second study, we presented a new neutral world that closely replicated the actual room where the individual was situated, so that participants would see the same environment when they put on or removed the head mounted display. Both subjective accounts of anxiety and physiological indicators of arousal indicated that it is indeed possible to design a truly neutral VR world that can be used for baseline measurements in therapy and research. Furthermore, despite reports in the literature, we did not find indications that the novelty of the virtual environment caused arousal (Wiederhold et al. 1998; Jang et al. 2002; Wiederhold and Wiederhold 2005) or that a virtual world would by definition generate arousal and anxiety (Wiederhold and Wiederhold 2005; Parsons and Rizzo 2008; Powers and Emmelkamp 2008).

Chapter 4

The research question in chapter 4 was whether anxiety sensitivity (AS) moderated the effects of somatic sensations and autonomic nervous system (ANS) reactivity on flight anxiety induced by actual flight. Results indicated no moderating effect of AS on the relationship between self-reported somatic sensations and flight anxiety. However, physiological reactivity did interact with AS: changes over flights in HR and parasympathetic activity were associated more strongly with flight anxiety changes from pre-treatment to post-flight for participants with high AS, and less strongly for participants with low AS. This seems to contradict results from chapter 2, in which aviophobic participants who scored high on anxiety sensitivity did not report more distress than phobics who scored low on this trait, even when showing stronger physiological responses to a video with flight-related material. Differences in outcome may be due to the low ecological validity of the video stimulus that generated only mild physiological reactivity (chapter 2), whereas participants in chapter 4 showed great physiological reactivity to actual flight. The absence of a moderating effect of AS on somatic sensations in both studies could be due to a ceiling effect. Aviophobics generally score high on reporting somatic sensations related to flight, as was also the case in these studies.

Chapter 5

The focus of the study in chapter 5 was on (changes in) cognitive coping in relation to long-term treatment outcomes. Results indicated that the pre-treatment use of cognitive coping strategies was not predictive of therapy outcome. However, participants were in a long-term process of change that, even in cases of maladaptive cognitive coping strategies, continued positively after therapy. Aviophobic participants showed clinically significant improvement in cognitive coping strategies, from pre-treatment scores matching those of dysfunctional populations to post-treatment responses matching those of a normal population. A greater increase in the use of adaptive coping strategies, and more importantly, a greater decrease in the use of maladaptive coping strategies during therapy were indicative of less long-term relapse of flight anxiety and more flights flown within three years after treatment. To our knowledge this is the first study to report the predictive value of changes in coping strategies during treatment for subsequent clinical change within the anxiety domain.

Chapter 6

This study examined the notion that fear activation and habituation during exposure to flight (related) stimuli are indicators of successful emotional processing and therefore predictive of treatment outcome. Participants showed strong fear activation during simulated and actual flight, combined with diminishing physiological and subjective responses. However, results only partially corroborated the EPT expectations. HR habituation during the first exposure flight, and increase in parasympathetic activity over the second exposure flight, were predictive of less flight anxiety on the short-term, but not of flight anxiety three years after finishing therapy, or of long-term flying behaviour. Within-session and between-session habituation of self-reported distress was not associated with treatment outcome. These results correspond to findings of a recent systematic quantitative review of the association of the three EPT process variables (IFA, WSH and BSH) and indicators of treatment outcome after exposure therapy for people diagnosed with an anxiety disorder (Rupp et al. 2016); BSH and WSH were (not significantly) positively related to treatment outcome, while IFA was not associated with outcome. Physiological process measurements led to higher correlations with treatment outcome than did self-report measurements and were regarded to be more valid indicators of fear network activation. Positive treatment outcome in this review was defined as any improvement in pre-post difference scores. No details were provided on the timing of post-treatment measurements.

Chapter 7

The research question in chapter 7 was whether synchronous change in subjective and physiological reactivity over repeated exposures increased with the intensity of emotional stimuli, and whether the magnitude of synchronous change during treatment predicted short- and long-term treatment outcome. Very few studies have reported evidence of synchrony, despite the recent growth of interest in the relationship between emotional expression and patterns of ANS activity (Hollenstein and Lanteigne 2014; Levenson 2014a; Benoit Allen et al. 2015). It was thought that this was caused by the generally low intensity and low ecological validity of the stimuli used. Results in the present study, despite the broad range from low intensity video-stimuli to intense phobic fear provocation during actual flight, did not show a relationship between the intensity of the phobic stimuli and the magnitude of synchronous change in subjective and physiological reactivity. Furthermore, results provided no support for the functionalistic view that successful treatment of anxiety disorders is indicated by synchronous change across emotional response systems. Participants showed marked subjective and physiological reactivity, and marked changes across repeated exposures, especially in the actual flight condition. Nevertheless, at group level, these intense and ecologically very valid stimuli did not evoke synchronous change in self-reported and physiological reactivity. Within-subject synchronous change in the two systems was not indicative of short-term and long-term treatment results.

DISCUSSION OF RESULTS

People with aviophobia do not form a homogeneous group. Aviophobia is a heterogeneous phenomenon with large individual differences in the onset and acquisition of the phobia, severity of symptoms and above all comorbidity with other phobias and other anxiety disorders. The empirical research in this thesis focused on individual differences in subjective- and physiological reactivity to flight (related) stimuli. Results of these studies are mixed and difficult to fit into existing theoretical models. As often the case, results from empirical studies add complexity to attractive theoretical perspectives. Our results did not corroborate the expectations derived from emotional processing theory. Neither did results support the evolutionary and functionalistic view that the magnitude of synchrony between emotional response systems is an indication of successful treatment outcome.

Aviophobic participants showed large subjective fear reactivity to videos with flight related material, simulated flight and actual flight, and large within-session and between-session habituation of subjective fear reactivity during simulated flight and actual flight. However, only individual subjective fear reactivity shortly before actual flight exposure, and subjective fear reactivity during actual flight, were related to post-flight and long-term treatment outcome.

Aviophobic participants showed a much stronger variation in the direction of heart rate reactivity and parasympathetic reactivity to the video stimuli than did control participants without aviophobia. This led to the conclusion that before the start of treatment some participants reacted with a typical flight-fight response, while others reacted with a prototypical passive coping response (freeze). Psychophysiological reactivity to the video stimuli was not predictive of treatment outcome. Participants showed strong physiological fear activation during simulated and actual flight, and significant within-session and between-session habituation of physiological reactivity during simulated and actual flight. Heart rate habituation during simulated and actual flight, and increase of parasympathetic activity over actual flight, were associated with less flight anxiety on the short-term, but not with flight anxiety three years after finishing therapy, or with long-term flying behaviour. Heart rate reactivity at the end of in-vivo exposure was the only physiological variable that was associated with long-term treatment outcome.

Anxiety sensitivity did not moderate the relation of self-reported somatic sensations with flight anxiety during flight, however the relation of HR and parasympathetic reactivity with flight anxiety was stronger in participants with higher levels of anxiety sensitivity. The addition of physiological markers of arousal strengthened the model of cognitive misinterpretation of bodily sensations (chapter 4). Furthermore, the addition of physiological markers of arousal led to the conclusion that a supposedly neutral VR world was not neutral after all (chapter 3), an inference that had not been possible only with subjective indications of anxiety.

Sympathetic reactivity, as measured by pre-ejection period, showed no relationship with short- or long-term treatment outcomes. This could indeed indicate that changes in sympathetic activity are not related to outcomes of therapeutic interventions. Or it could indicate that in the present research we did not effectively capture sympathetic activity. Although the PEP is currently the measure of choice for psychophysiological stress research in real life settings (Goedhart et al. 2006; Neijts et al. 2015), it has several disadvantages. Scoring requires identification of the onset of the Q wave, which can be

ambiguous. In about 20% of all recordings the Q wave is not clear, or even visible (Lien et al. 2015). Recently, research on two alternatives for the PEP has emerged. Lien et al. (2015) reported on the ECG-T wave amplitude (TWA) as an alternative ambulatory sympathetic measure. The TWA requires only an ECG signal, making it even less cumbersome for participants than a PEP measurement that requires a combination of ECG and ICG. Furthermore, the TWA requires less laborious visual scoring and seems more open to automation than PEP scoring. TWA could be reliably extracted in over 90% of a group of 564 healthy adults being followed for 24 hours. However, within-participant changes in TWA and PEP correlated significantly in only 75% of the participants. A second, more promising, alternative might be to use the R peak instead of Q-onset to calculate PEP. The R peak is the clearest component of the ECG and is easily and precisely identifiable (Sherwood et al. 1990). Like TWA, the R peak is also more amenable to automated identification than is the onset of Q. In several laboratory experiments with a total of 408 healthy young adults, Seery et al. (2016) examined the relationship between PEP based on Q identification and PEP based on R identification. Absolute levels of R-peak defined PEP accounted for nearly 90% of the variance in absolute levels of traditionally defined PEP. More importantly, within-person reactivity R-peak defined PEP accounted for over 98% of the variance in traditionally Q-defined PEP. However, responses were measured during resting or minimally metabolically demanding tasks, thereby limiting generalization. Future research under naturalistic and ambulatory conditions seems warranted. Sympathetic activity in the present dissertation was assessed by a traditional scoring method using the onset of the Q wave.

Higher vagal tone and greater vagal withdrawal during challenge have been associated with a better ability to engage with and disengage from environmental demands, and reduced HRV and reduced vagal tone have been associated with anxiety (Friedman 2007; Chalmers et al. 2014). Lower vagal control has been linked to less adaptive emotion regulation. Mathewson et al. (2013) report that greater RSA reactivity (appropriate parasympathetic withdrawal to manageable stress) was associated with greater reduction of self-reported social anxiety. High levels of adaptive variability, as e.g. indicated by respiratory arrhythmia, characterize a healthy autonomic nervous system, although Beauchaine (2015) reports that excessive RSA reactivity (i.e. withdrawal) to emotional challenge is associated with symptoms of psychopathology. There is increasing evidence that non-specific vulnerability to psychopathology is reflected by low resting RSA and excessive reduction in RSA during emotion evocation, through prefrontal cortex feed-forward and feedback connections with the amygdala (Beauchaine 2015). RSA could be a transdiagnostic biomarker of emotional dysregulation, consistent with the

Research Domain Criteria (RDoC), that classifies psychopathology based on dimensions of observable behaviour and biological measures instead of traditional categorical and symptom-oriented diagnostic criteria (Lang 2014; Beauchaine 2015; Nees et al. 2015). Aviophobic participants in the present study showed a much stronger variation in the direction of cardiac parasympathetic reactivity than controls when exposed to a video with flight-related stimuli (chapter 2). Increased parasympathetic habituation over actual flight was associated with less reported flight anxiety after flight (chapter 6), while results from chapter 4 indicate that lower RSA reactivity over actual flights was associated with a stronger decrease in flight anxiety from beginning to end of therapy. In view of these mixed outcomes it seems that RSA reactivity is neither a valid and reliable diagnostic instrument to classify aviophobia, nor a reliable indicator of progress of therapy and therapy outcome for people with severe fear of flying. Further research seems warranted to examine whether HRV can supplement standard outcome measures in the treatment of aviophobia. Additionally, HRV could also be the target of intervention, based on the idea that improved HRV parameters are associated with less distress (Friedman 2007; Lehrer and Gevirtz 2014). Future research on HRV targeted intervention with people with aviophobia also seems warranted.

Heart rate is the resultant of sympathetic and parasympathetic control on the intrinsic rate of the cardiac pacemaker. HR itself does not reveal the sympathetic and parasympathetic ANS cardiac activity. Nevertheless, HR turned out to be a better predictor of treatment outcome than RSA and PEP. Higher HR habituation over actual flight predicted stronger decrease in flight anxiety from beginning to end of therapy (chapter 4 and chapter 7) and less flight anxiety after the exposure flight (chapter 4, and chapter 6). Furthermore, participants with a greater decrease in HR over simulated flight reported a greater decrease in flight anxiety from beginning to end of therapy than participants with less diminution of HR over the simulated flights (chapter 7). Finally, HR turned out to be the only physiological variable associated with long-term treatment outcome; lower HR reactivity at the end of the exposure flights was associated with less flight anxiety three years after treatment. The combination of HR reactivity still present after in-vivo exposure with SUD reactivity just before in-vivo exposure explained 29% of the variance in reported flight anxiety three years after treatment (chapter 6). Interestingly, these prognostic variables for long-term treatment outcome were all centred around in-vivo exposure. Although Seligman's (1971) proposition that phobias are highly resistant to extinction has been proven wrong (e.g. Ost et al. 1997), he correctly noted that phobias seem quite resistant to change by "cognitive means" alone (McNally 2016).

Cognitive changes during therapy proved highly influential for therapy outcome (chapter 5). Participants showed clinically significant improvement in cognitive coping strategies, from pre-treatment scores matching those of dysfunctional populations to post-treatment responses matching those of a normal population. Individual differences in changes in coping style during treatment until short-term follow-up were predictive of changes in flight anxiety from short-term follow-up to 3 years later. The additional explained variance in flight anxiety by changes in primarily maladaptive coping style over and above changes in flight anxiety during treatment was 21%. The additional explained variance of flights taken by changes in adaptive and maladaptive coping style over changes in flight anxiety was 12% (chapter 5). Participants in this study followed CBT, with cognitive therapy preceding behavioural components, including exposure in-vivo. Studies on the additive value of cognitive interventions report mixed results; some studies reported enhanced treatment outcomes when cognitive interventions were added to behavioural treatment, whereas others reported no effects (for details see Raes et al. 2011 page 965; Ramnero 2012; Wolitzky-Taylor et al. 2008). For example, one of the few studies that investigated the ancillary support of cognitive interventions during CBT for specific phobias randomly assigned 31 spider phobic participants to graded exposure with or without cognitive interventions (Raes et al. 2011). Both groups benefited equally from treatment, and both groups showed a nearly equal decrease in phobia-related cognitions. Attrition rates seem to benefit from a combination that includes cognitive interventions (Ramnero 2012).

Delineating the effect of individual treatment components of CBT has been proven difficult. It is conceivable that fear extinction might take place by different pathways or mechanisms: either by behavioural pathways through exposure, or via cognitive pathways through cognitive restructuring. Another conceivable pathway is a combination of both mechanisms, in which each mechanism strengthens the other. Cognitive interventions facilitate exposure; subsequent exposure facilitates cognitive change, diminishing avoidance and lowering the threshold for further exposure that in turn will lead to additional cognitive change, and so on in a self-reinforcing process.

We did not relate changes in coping to psychophysiological arousal. Luck and Lipp (2015), in a study on instructed extinction with 80 healthy undergraduate students, reports that negative valence acquired during fear conditioning might be less responsive to cognitive interventions, while physiological indices of fear learning responded well to the same cognitive intervention. If residual negative valence persists after extinction, relapse of fear is plausible when the person is put in a high arousal situation (Kerkhof et al. 2011;

Zbozinek et al. 2015). Future research on the association of physiological markers of fear and changes in coping style over therapy could shed light on the differential time paths of fear extinction, as well as the possible use of biomarkers as indicators of cognitive treatment gains and predictors of relapse.

Interestingly, in our study higher levels of self-reported fear pre-exposure, but not physiological indicators of fear pre-exposure, were related to poorer long-term treatment outcome (chapter 6). High levels of anticipatory self-reported fear pre-exposure could indicate that participants are not yet ready to face their phobic fear; this may lead to (cognitive) avoidance. Avoidance is a maladaptive coping style that is strongly associated with negative treatment outcome and may constitute an important maintaining process in phobias (Hendriks et al. 2013; Boettcher et al. 2016; Spinhoven et al. 2016). If participants are no longer able to tolerate their phobic anxiety during exposure, extinction learning will not take place (Bouton 2004; Craske et al. 2008). The association of higher self-reported distress activation during the first exposure flight with higher levels of flight anxiety after exposure, and fewer flights flown in the three years after therapy, might as well be an indication of experiential avoidance impeding successful emotional processing.

STRENGTHS AND LIMITATIONS

A major strength of the studies described in this thesis is the use of a relatively large clinical sample of participants seeking treatment, in combination with in-vitro and in-vivo exposure and concurrent physiological measurement. Very few studies have been published with comparable numbers of clinical aviophobic patients undergoing real life exposure, and if so, mostly are without psychophysiological assessment. Chapter 4 gives a comprehensive overview. Oakes and Bor (2010) also provide an extensive review of fear of flying intervention studies with and without physiological assessment. Another positive feature of the studies is the use of two entirely different clinically relevant long-term outcome measures: a self-report measure indicating flight anxiety and a behavioural measure indicating flight behaviour.

All studies in this thesis were conducted at a treatment facility, not at a research facility. Participants were highly anxious aviophobics who applied for treatment, and all participants paid for their treatment. Although this setting considerably limited the research options, at the same time it produced ecologically highly valid results. Stress

induced in a laboratory setting is by definition artificial. However, laboratory-based research facilitates multimodal assessment that makes it possible to capture variations that might not be apparent when using a limited number of measures in ambulatory conditions. We used the VU-AMS (www.vu-ams.nl) to record ECG and ICG unobtrusively and continuously during all phases of the treatment process, including actual flight. All questionnaire data were collected before or after therapeutic interventions and experimental conditions; only during flight was there a perfect overlap between physiological recording and the verbally administered SUDs. New technological developments enable Ecological Momentary Assessment (EMA) procedures that assess emotional state by means of tablets and smartphones to overcome the retrospective reporting bias when emotional state is assessed retrospectively (Conner and Barrett 2012). Furthermore, EMA provides possibilities to study emotion regulation in the complex context of everyday life. Most laboratory-based studies have focused on regulation of specific emotions in isolation (Aldao and Tull 2015; Sims et al. 2015). Emerging technologies, however, allow for concurrent multimodal psychophysiological, subjective, and behavioural assessments in ambulatory, naturalistic settings (Seeley et al. 2015). We analysed physiological data off-line after the therapeutic intervention or experimental condition. The VU-AMS has an event marker and an integrated accelerometer. Both the therapist and the accompanying pilot kept a detailed log during both exposure flights. All these resources were used to select movement-free and artefact-free periods that lasted at least 5 minutes each as close as possible around the times when the SUDs were collected. Still, some HR, RSA and PEP changes could have been caused by metabolic needs, although during flight, when patients sit quietly, physiological activation is mainly caused by perceived stress and not physical activity (Roth 2005). Promising new ambulatory technologies and new algorithms allow for assessment of changes in cardiac parameters that are not due to metabolic needs. Verkuil et al. (2016) provided a proof of principle in a healthy sample of 51 young students. After a short person-specific calibration procedure (including sitting, standing, lying down, cycling and climbing stairs, totalling 15 minutes) participants provided cardiac measures by wearing a chestbelt for 24 hours, and self-report data that were collected hourly with the use of a smartphone. With the help of an automated algorithm the researchers were able to distinguish between prolonged metabolic and non-metabolic HRV reductions in daily life. These and other new techniques would allow for higher sample rates without causing too much of a nuisance for the patients. In our study both exposure flights lasted approximately one hour. The cruise portions of these flights were not long enough to furnish multiple movement-free measurements in the physiological domain in combination with a SUD measurement, without interfering the therapeutic process. Multiple measurements

during flight might have provided better indications of within-session habituation.

Reported success rates of treatment of aviophobia are generally higher than those reported for other anxiety disorders (Van Gerwen et al. 2004; Oakes and Bor 2010). Phobic participants are typically highly motivated and expect the therapy to be effective. Even when not cured of their fear, most of them would report improvement after investing so much in terms of time, money and emotions. This is reflected in outcomes reported by many programmes. Tests of effectiveness based on measures like number of participants taking a "graduation" flight or scores on the severity of anxiety directly after therapy are bound to be overly positive. One could argue that the reported high success rates do not adequately represent effectiveness, but merely indicate motivation and stamina to complete the program. In the current studies, we used self-reports of flight-anxiety and measurements of actual behaviour three years after finishing therapy. Ideally, positive outcome should be reported as clinically significant improvement, defined as pre-treatment scores matching those of dysfunctional populations to post-treatment responses matching those of a normal population (with an additional margin to compensate for individual subjects' measurement error (Jacobson and Truax 1991; Hinton-Bayre and Kwapil 2017)). Additional assessment before, during and after treatment would have enhanced the research and analytic possibilities and could have provided more indications of clinically significant improvement. However, as noted before, the research setting considerably limited the options. Although we were able to add a few paper-and-pencil questionnaires to the regular battery of questionnaires used in the diagnostic phase, our effort to include the MINI or other structured diagnostic interviews was not honoured. The semi-structured interview during the diagnostic phase yielded information on the present situation and personal history of the participants; it also included questions about other phobic complaints and present emotional state. Moreover, additional questions were included to assess life events during the onset of the flying phobia, information on flying behaviour, flying history, and the phenomenology and determinants of the subjects' fear of flying, Future research on the relationship between these dimensional variables and long-term outcomes of therapy seem warranted.

Adding extra questionnaires or procedural steps during treatment was not a viable option, and we did not want to burden the participants unnecessarily afterwards. Furthermore, for the 3-year follow-up we had to make a trade-off between probability of response and completeness of data. A 1-year follow-up using written questionnaires with participants from the same treatment facility had previously yielded response rates

of only 50%. In order to increase the probability of response in the present studies, we decided to use a very limited number of questions for the 3-year follow-up. As it is, we are satisfied with the high response rate of 85%. Nevertheless, additional assessment could have provided data for cross-legged panel design analyses. It would be very interesting to conduct a 10-year follow-up with the same group of participants. A comprehensive assessment would definitely ameliorate the analytic possibilities.

Another limitation is that we did not assess additional treatment or the use of alcohol, drugs, and medication between end of treatment and 3-year follow-up. During individual treatment and during the 2-day group therapy, participants received information on the use of alcohol, drugs and medication in relation to anxiety. Participants were made well aware that avoidance behaviour and cognitive avoidance are detrimental for maintenance of their treatment gains, and they were well informed that the use of these substances is equal to avoidance. At the end of treatment participants were urged to make a flight within three months. At the short-term follow-up (three months after end of treatment), 98% of the participants reported that they had indeed made a flight, without the use of alcohol, drugs or medication. However, at the 3-year follow-up we did not explicitly ask participants whether they had sought additional treatment or made use of medication, drugs or alcohol during the flights they self-reported. We left space for comments on the reply form. None of the responders reported additional treatment or the use of medication, drugs or alcohol during the flights. A future follow-up study would do well to include these topics.

Individual behaviour is influenced by the presence of others, and group dynamics is part of cognitive-behaviour group therapy. Group-based treatment has consequences for how individuals respond to treatment within many settings. Participants in the present studies started group-based treatment after the phase of individualized treatment. Group treatment, apart from its beneficial financial aspect, aids the participants in imparting information, gaining self-understanding, and sharing emotions. Additionally, cohesiveness helps them to minimize avoidance behaviour, especially shortly before the in-vivo exposure flights at the end of CBGT. These dynamics could partly explain the high percentage of participants boarding the exposure flights, and might be one of the reasons for the high success rate reported by many other studies on aviophobia. However, it seems unlikely that being part of a group did critically influence the independent and dependent measures used in the studies included in this thesis. SUD-scores were collected privately; members of the group were not aware of each other's scores on this questionnaire. Nevertheless, group-dynamics could have influenced these scores. We

therefore quantified the individual differences in fear activation during exposure to the phobic stimuli as the changes in subjective distress scores and physiological arousal over an appropriate baseline. Short-term effect of therapy outcome was operationalized as the flight anxiety score taken just after the second exposure flight, and again taken privately. Long-term effect of therapy outcome was operationalized as the flight anxiety scores three years after treatment, and number of flights taken in this three-year period. Email was used to gather these data. It is difficult to conceive how group-dynamics could have influenced these data. However, it could be argued from a statistical point of view that we collected repeated measurements on individuals who are nested (or clustered) within (treatment) groups, while we used statistical models (such as ANOVA and linear regression) that assume independent observations. However, given our relatively limited sample size, we refrained from performing statistical analyses such as multilevel models or hierarchical linear models that do not assume independence of observations.

The studies described in chapters 2 and 3 included participants with and without aviophobia; no other studies included control groups or control conditions. Repeating the experiments on non-phobic "regular" flyers would be very problematic, as these experiments place a substantial burden on participants (airport security, inflight measurement, additional visits to a simulator and sessions for video exposure). In addition, including a no-treatment control condition is not feasible as most participants with aviophobia in a no-treatment control condition will not be able or willing to take a test flight resulting in unacceptable high attrition rates. The specific nature of the treatment in combination with a focus on prediction of long-term outcome based on individual differences in reactivity justifies a within-person design. Furthermore, the considerable changes in flight anxiety, flight behaviour, and cognitive coping (chapter 4) during treatment make it unlikely that these changes in a sample with protracted complaints are merely the results of passage of time or repeated testing. Nevertheless, the study design made it difficult to delineate the effect of individual treatment components. Other limitations to mention are the high attrition rate and missing data. As already described in the separate chapters, we performed extensive missing value analyses on all available physiological variables, as well as on all available questionnaire data and sociodemographic characteristics. Furthermore, when possible, analysing strategies were used that proved robust in dealing with missing cells in repeated-measures data.

CLINICAL IMPLICATIONS

In-vivo exposure is clearly the most important aspect in the treatment of aviophobia. Nevertheless, ancillary therapies could effectively optimize exposure-based interventions and will ultimately result in better short-term and long-term treatment outcomes (Pittig et al. 2016). Flanking enhancement strategies that support preparation and post-exposure processing might facilitate exposure and boost the effect of exposure treatment. Procedural enhancement strategies implemented during actual exposure focus on optimizing fear extinction by maximizing the identification of the mismatch between threat expectancies and actual outcome.

The clinical efficacy of interoceptive exposure for anxiety disorders has been well established (Khalsa and Lapidus 2016), and cognitive restructuring in combination with interoceptive exposure exercises is known to be efficacious in reducing AS (Smits et al. 2008; Boettcher et al. 2016). As problematic interpretation of physiological sensations is profoundly common in many anxiety disorders, interoceptive exposure (IE) could be a helpful transdiagnostic intervention (Boettcher et al. 2016). The processing of disconfirmatory evidence offers patients the opportunity to learn that bodily sensations are not in themselves danger signals. Maximizing opportunities to learn that feared outcomes are less severe than expected, or less likely than expected, and that fear itself is tolerable, requires intense delivery of IE, without arousal-reduction strategies and no between-trial rest periods (Deacon et al. 2013). However, despite the overwhelming evidence of the efficacy of exposure-based treatment, many self-described cognitive-behavioural therapists make infrequent use of therapist-assisted exposure, or even totally omit this most important ingredient (Hipol and Deacon 2013; Powers and Deacon 2013). Hipol and Deacon (2013) report that psychotherapists in the state of Wyoming use IE only sparingly (3% - 12%), although psychotherapists who advertise themselves as specialists in the treatment of anxiety disorders use interoceptive exposure significantly more often (25% - 40%). Although its value is evidence-based, IE is a vastly untapped resource for treatment (Boettcher et al. 2016).

Pre-exposure cognitive interventions aimed at disconfirming maladaptive beliefs and reducing fear may lower the threshold for subsequent exposure, and may prevent cognitive avoidance and disengagement during exposure (Blakey and Abramowitz 2016). Exposure to a feared object or situation without catastrophic consequences provides the phobic individual with an opportunity for corrective experiences and inhibitory learning. Pre-exposure cognitive interventions may boost this effect during exposure by focusing

attention on the discrepancy between maladaptive cognitions and the actual outcome.

The relationship between emotional response systems (chapter 7) is likely affected by many intervening variables, including higher order cognitive processes. We judge and feel emotions about our emotions. Perceiving an emotion as unacceptable, problematic, or aversive instead of normal, can influence the way a person regulates the emotional state itself (Schaefer et al. 2014; Couyoumdjian et al. 2016). A conflict between uncontrollable, automatic phobic reactions and the recognition that the phobic fear response is irrational and even embarrassing may lead to an increased attempt at emotion regulation, in an effort to suppress or control the fear reaction (Schaefer et al. 2014). The time course of emotion subsystems may vary greatly (Hollenstein and Lanteigne 2014; Levenson 2014b), and may vary even more owing to this additional cognitive regulation. Higher order cognitive processes may therefore intervene with the supposititious temporal associations between responses (Mauss et al. 2005; Schaefer et al. 2014). If a side effect of pre-exposure cognitive therapy is a reduction of automatic and coherent responses between domains, then this might lead to a lagged or reduced physiological fear response (Schaefer et al. 2014). Blunted physiological fear responses might diminish the effectiveness of (in-vivo) exposure therapy, as according to emotional processing theory, fear activation is a prerequisite of fear-extinction (Foa and Kozak 1986). Cognitive interventions, aimed at alleviating fear or at promoting regulating strategies that dampen automatic and coherent responses, might therefore better be postponed to after the exposure component of the treatment (Craske et al. 2014b).

Pre-exposure flanking strategies aimed at fear tolerance may aid in reducing avoidance behaviour and may promote extended confrontation with the feared object or situation during exposure. For example, Acceptance and Commitment Therapy (ACT) has shown promising results in facilitating engagement in subsequent exposure, thereby maximizing the mismatch effect when expected aversive events do not happen (Meuret et al. 2012; Roemer et al. 2013; Craske et al. 2014b). Several meta-analyses provide cumulative evidence for the efficacy of this transdiagnostic approach in the treatment of anxiety, with comparable outcomes for CBT and ACT (Craske et al. 2014a; Ost 2014; Landy et al. 2015; Hacker et al. 2016). Distress tolerance might be a moderator in exposure therapy (Asnaani et al. 2016). However, ATC as a stand-alone therapy is liable to high dropout rates (Arch et al. 2012; Dahlin et al. 2016). Emerging technologies allow for pre-exposure flanking therapy at home, with minimal therapist interaction. ATC can be delivered by means of interactive online modules and smartphone assisted guidance (Dahlin et al. 2016; Ivanova et al. 2016). A specialized treatment facility in the Netherlands

developed a mobile phone Flight App with functionalities that diminish pre-flight distress and reduce avoidance tendencies (VALK Fear of Flying App; https://itunes.apple.com/nl/app/fear-of-flying-app/id501475441). The app is available in several languages and has been downloaded over 17.000 times. Hartanto et al. (2015) developed a new home-based VRET system that could be used as pre-in-vivo-exposure aid. The system includes HMD, HR sensor, microphone, laptop, and a system manual that guides patients through various steps of therapy. Therapists can monitor progress remotely and can amend their treatment plan. SUD's and HR are available to determine anxiety level.

Several procedural enhancement strategies are available. First of all, most anxiolytics like benzodiazepines are known to impair fear extinction and should, as far as possible, be banned during the therapeutic process (Wilhelm and Roth 1997; Singewald et al. 2015). Benzodiazepines provide short-term relief but significantly diminish the effects of treatment for anxiety and hinder long-term effects of extinction (Graham et al. 2014). Pharmacological agents that work as cognitive enhancers (d-cycloserine, oxytocin, yohimbine et cetera) have gained considerable attention lately (see Hofmann et al. 2015a for a concise review, and; Singewald et al. 2015 for a more extensive review). D-cycloserine has shown promising results during CBT, although the optimal dosing and dose timing proved difficult (Hofmann et al. 2015b; Otto et al. 2016). The agent enhances cognitive processes not only during extinction learning but also augments fear memory reconsolidation (Hofmann 2014 "making good exposures better and bad exposures worse").

Non-pharmacological procedural strategies are mostly aimed at increasing threat expectancies to augment their violation. For example, removal of safety signals and safety behaviours will increase threat expectancies and augment extinction learning because the mismatch between expected catastrophic outcome and actual outcome is not associated with the safety signals and behaviours (Craske et al. 2014b). Increasing the variability and context of extinction training facilitates maintenance of treatment gains and supports relapse prevention (Laborda et al. 2011; Swan et al. 2016). External functional mediators may facilitate treatment gains and generalization of gains. For example, a telephone app designed to be used during in-vivo exposure might prompt users to use the skills learned in treatment (Swan et al. 2016).

While exposure therapy generally advocates the removal of safety behaviours, recent publications focus on the beneficial effects of incorporating safety behaviours during exposure (Goetz et al. 2016; Meulders et al. 2016). For one, safety behaviours aid in

engaging and enduring exposures that without safety behaviour would not be tolerated, thereby giving the opportunity to generate non-threat associations (Goetz et al. 2016). The use of safety behaviours during exposure enhances the acceptability and tolerability of the intervention, and promotes greater distress tolerance (Blakey and Abramowitz 2016). A solution for dropout and refusal to undergo exposure therapy may involve the judicious use of safety behaviours (e.g. cell phones or the presence of other persons: social conversation is a safety behaviour) to enhance the acceptability of exposure-based interventions (Levy and Radomsky 2014; Goetz et al. 2016). The already mentioned mobile VALK Flight App features functionalities like relaxation exercises and a "panic button" that activates an audio message aimed at decreasing tension levels. Meulders et al. (2016), in a meta-analytic review, did not find compelling evidence to support either the removal or addition of safety behaviours during exposure. However, Goetz et al. (2016) in their review conclude that (restorative) safety behaviours that augment confrontation with a core threat do not interfere, whereas (preventive) safety behaviours that hinder engagement during exposure effectively blunt emotional processing and weaken the outcome of exposure interventions. However, most of the reviewed studies measured outcome during or directly after treatment or intervention; long-term treatment successes have not been reported (Goetz et al. 2016; Meulders et al. 2016). Safety behaviours performed in the absence of real threat do not increase survival and paradoxically could give rise to and maintain anxiety (Blakey and Abramowitz 2016). Safety behaviours and safety aids may infer imminent threat, increase perception of threatening stimuli, and direct attentional resources away from disconfirmatory information; "*if a safety aid is present, there must be danger*" (Blakey and Deacon 2015, page 264). To summarize, the use of safety behaviours at the beginning of exposure therapy might aid patients in engaging in exposure and enduring the temporary distress that is an inherent part of exposure treatment. Mobile technology might serve as a mechanism delivering safety signals that enhance willingness to endure the exposure. These technologies would allow for judicious use of safety behaviours, fading through consecutive exposures (Goetz et al. 2016). Balancing the opposing effects of safety behaviours and safety aids requires individualized tailored intervention strategies prior to, during, and after exposure (Pittig et al. 2016). Ultimately these safety behaviours should be eliminated to maximize the effect of exposure therapy (Craske et al. 2014b; Pittig et al. 2016).

Post-exposure coping interventions may be beneficial for reinforcing extinction learning and consolidating treatment gains (Vervliet et al. 2013; Craske et al. 2014b). Verbally going through the exposure experience after the actual exposure, and emphasizing the contrast between the anticipated outcome and the actual experience, can reinforce

extinction learning. This will strengthen the perceived ability to handle frightening situations, diminish avoidance, and consolidate treatment progress (Craske et al. 2014b; Clark and Rock 2016). Research on the therapeutic efficacy of post-exposure coping interventions is still in its infancy.

SUGGESTIONS FOR FUTURE RESEARCH

Most suggestions for future research have already been mentioned above, the most important are here recapitulated. To start with the most obvious one, a 10-year follow-up with the same group of participants would be very informative. This should involve a comprehensive assessment, also of additional treatment and the use of alcohol, drugs and medication before and during flight.

Integral to science are replication, expansion of existing work and refutation of previous findings. Emerging technologies and developments in software will facilitate ecological momentary assessment along with continuous physiological measurement in therapeutic settings without interfering with the therapeutic process. Hopefully these innovations will stimulate replication and expansion of the present research. Moving beyond cardiac parameters may provide additional information. Our results would suggest simplifying cardiac measurement to simply HR and HRV, thereby reducing complexity without losing content. Future research is needed to support (or refute) this proposition. HR and HRV can be measured easily and non-intrusively with modern smart watches. These devices would even allow for telemetric data transmission and real time physiological feedback. Research on HRV targeted interventions with aviophobic subjects seems warranted.

To deal with a multitude of underlying phenomena, treatment programs often use a combination of providing information, cognitive restructuring, relaxation training and graded in-vitro exposure, before moving on to in-vivo exposure. The content, timing and quantity of these ancillary therapeutic components definitely need attention. For example, although pre-exposure cognitive interventions lower the threshold for subsequent exposure, they may at the same time diminish the effectiveness of in-vivo exposure therapy by promoting regulating strategies that dampen automatic and coherent responses. On the other hand, pre-exposure acceptance and commitment therapy may help to facilitate engagement in exposure exercises without diminishing in-vivo exposure efficacy. Likewise, virtual reality exposure therapy (VRET) may assuage anxiety associated with upcoming in-vivo exposure. However, little is known about how

VRET affects efficacy of consecutive in-vivo exposure. Post-exposure cognitive therapy may help to consolidate treatment gains. Research is needed to optimise these flanking strategies.

Several available mobile phone apps claim to ease stress associated with flight. The "Am I going down" app is a risk calculator that provides the likelihood of a flight going down, the "ANA Takeoff Mode" app provides distraction through immersive gameplay, and the "Turbcast" app allow passengers to view a turbulence forecast along their flight route. However, these apps may increase rather than decrease anxiety before and during flight. More beneficial thoughts have been put into the "Flight Without Fear" and "SOAR" apps; both primarily offer information on take-off procedures, turbulence and aircraft maintenance. Nevertheless, only systematic assessment can provide data on the positive and negative aspects of these aids. Regrettably, the only available app based on scientific research has never undergone a scientific assessment; research on the VALK Fear of Flying App is long overdue. This app may promote and facilitate exposure, and diminish avoidance. On the other hand, it could be seen as a mechanism that delivers safety signals, thereby creating dependency. Future research would do well to assess these different attributes.

Very few passengers are completely comfortable during all phases of flight. A sudden jolt of turbulence alarms everyone. Very few people enjoy an approach in gusty wind conditions (though most pilots do!). Unexpected or "inexplicable" events during flight are quite common; some apprehension is an intrinsic part of flying for most passengers. After treatment the fearful flyer should be able to cope with these situations and the feelings associated with these situations. Clinical significant improvement means being able to deal with flight and all aspects associated with flight, not being perfectly comfortable all the time. Future research on efficacy of treatment would benefit from a wide array of normative data and better definitions of clinically significant improvement.

Disorder-specific treatments focus on differences rather than similarities in the treatment of disorders; transdiagnostic treatments focus on the similarities in etiology and common underlying factors of various anxiety disorders. Transdiagnostic CBT may have practical advantages over traditional CBT when group therapy participants are diagnostically heterogeneous; this is the case with aviophobics who have a multitude of underlying pathologies. Determining which combination of disorder-specific interventions and transdiagnostic interventions is most effective in this clinical setting is a great challenge, and requires continuous research. Such research would benefit

from the use of psychophysiological measures, as assessment of self-report disrupts whatever is going on; moreover, retrospective assessment of patients' own verbal report is notoriously unreliable. However, interpretation of physiological data is not clear-cut and also warrants additional research.

CONCLUSION

Pre-treatment individual differences in subjective distress reactivity and physiological reactivity to flight related stimuli, and pre-treatment use of cognitive coping strategies were not prognostic of short- and long-term post-treatment clinical course. In the course of therapy, individual reactivity became more strongly related to treatment outcome. The magnitude of change in the use of maladaptive coping strategies during therapy was indicative of long-term persistence of flight anxiety and number of flights flown within three years after treatment. Subjective distress reactivity, pre-exposure and during actual flight, was prognostic for short- and long-term treatment outcomes. Adding measurements of physiological reactivity improved the prediction of treatment outcome. The magnitude of synchronous change in subjective and physiological reactivity did not increase with higher intensity of phobic stimuli, and was not related to outcome. Subjective and physiological measurements of fear activation provided partly independent information. Prognosis for clinical course of aviophobia therefore could benefit from including physiological reactivity measurements.

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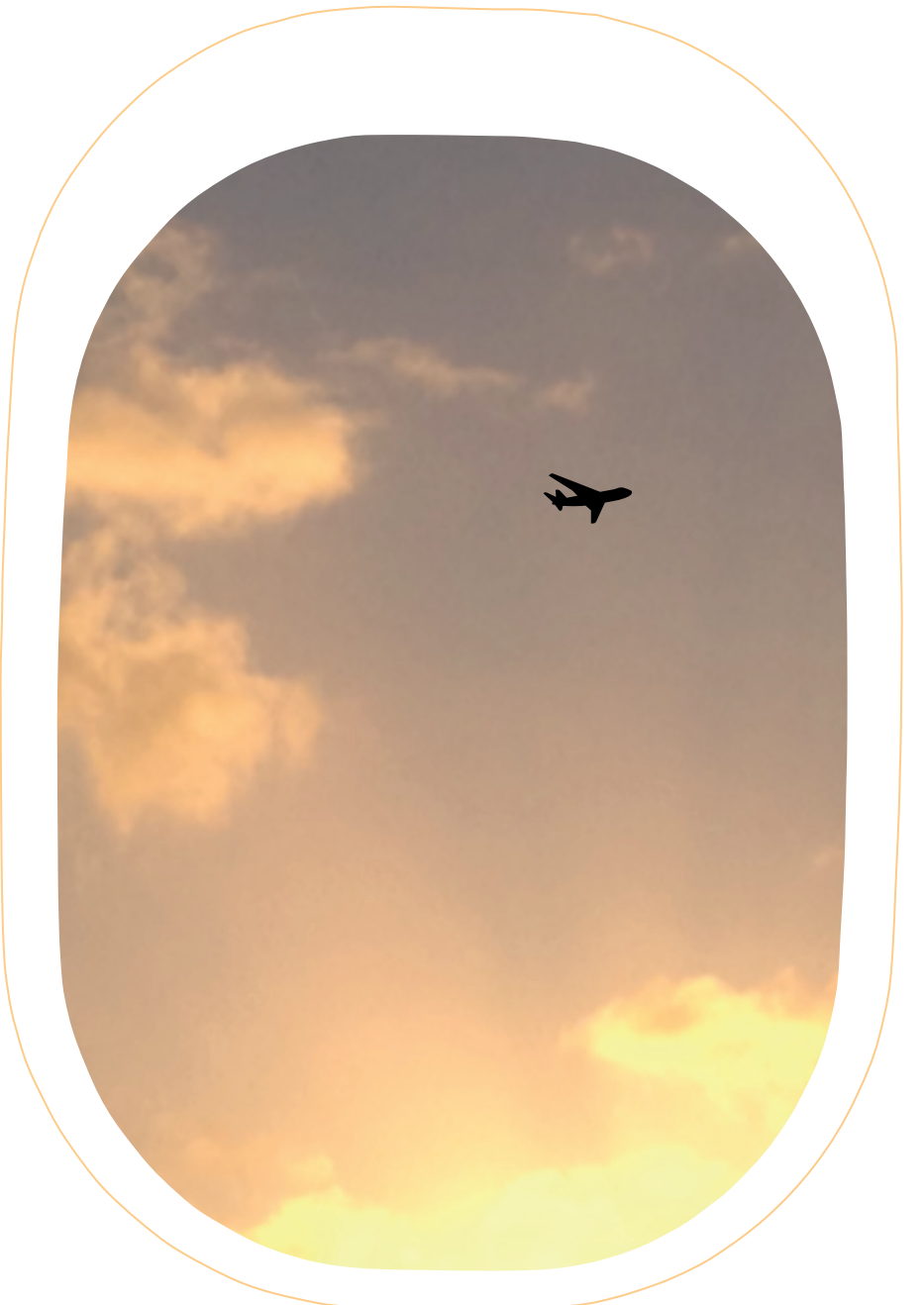


Nederlandse samenvatting

NEDERLANDSE SAMENVATTING

Hoofdstuk 1: De hoofddoelstelling van de in dit proefschrift beschreven empirische studies was het vergroten van de beschikbare kennis over individuele verschillen in subjectieve en fysiologische reactiviteit op vlucht gerelateerde stimuli bij mensen met ernstige vliegangst. Een tweede doelstelling was om de toegevoegde waarde van psychofysiologische metingen voor de diagnose van vliegangst en de prognose van het behandelingsresultaat te onderzoeken. Deelnemers aan het onderzoek waren mensen met vliegangst die zich bij een gespecialiseerd behandelingsinstituut hadden aangemeld om hun vliegangst te overwinnen.

Angst is functioneel, fobieën zijn dat niet. Vliegangst (fear of flying, FOF) is een aanhoudende en hevige angst tijdens of voorafgaande aan een vlucht. Deze angst en de ermee gepaard gaande vermijding staan niet in verhouding tot het daadwerkelijke gevaar en veroorzaken klinisch significante stress of beperkingen. Meer dan 1 op de 3 mensen vindt vliegen moeilijk en stressvol, tien tot vijftien procent van de westerse bevolking heeft vliegangst. Bijna al deze mensen vermijden vliegen, of vliegen met behulp van medicatie, drugs of alcohol. De voorkeurbehandelmethode is cognitieve gedragstherapie in combinatie met in-vivo exposure. Vaak wordt gebruik gemaakt van groepsbehandelingen met meerdere behandelcomponenten om een veelheid aan onderliggende stoornissen te bereiken. Hoewel sommige therapieonderdelen niet voor alle individuele deelnemers vereist zullen zijn levert deze transdiagnostische benadering vaak de beste resultaten.

Hoofdstuk 2: In dit onderzoek werd de relatie tussen subjectieve en fysiologische reactiviteit onderzocht bij deelnemers met FOF en controleproefpersonen zonder FOF. Na het bekijken van een video met vlucht gerelateerde stimuli rapporteerden proefpersonen met vliegangst significant hogere niveaus van subjectieve angst dan controleproefpersonen. Daarentegen verschilden in het algemeen de metingen van de drie fysiologische variabelen (hartritme, parasympathische reactiviteit en sympathische reactiviteit) niet tussen de twee groepen, hoewel bij deelnemers met vliegangst de parasympathische reactiviteit een grotere variabiliteit vertoonde. Angstgevoeligheid (anxiety sensitivity, AS) beïnvloedde de relatie tussen zelfgerapporteerde angst en fysiologische indicatoren van angst niet.

Hoofdstuk 3: Dit hoofdstuk beschrijft twee studies naar de mogelijkheid van baselinemetingen in Virtual Reality (VR). De resultaten gaven aan dat het mogelijk is om

een werkelijk neutrale VR-wereld te ontwerpen die kan worden gebruikt als baseline in therapie en onderzoek. De toevoeging van fysiologische indicatoren van angstactivering aan zelfrapportage maten voor angst leverde informatie op die essentieel was voor een correcte interpretatie van de neutraliteit van de virtuele omgeving.

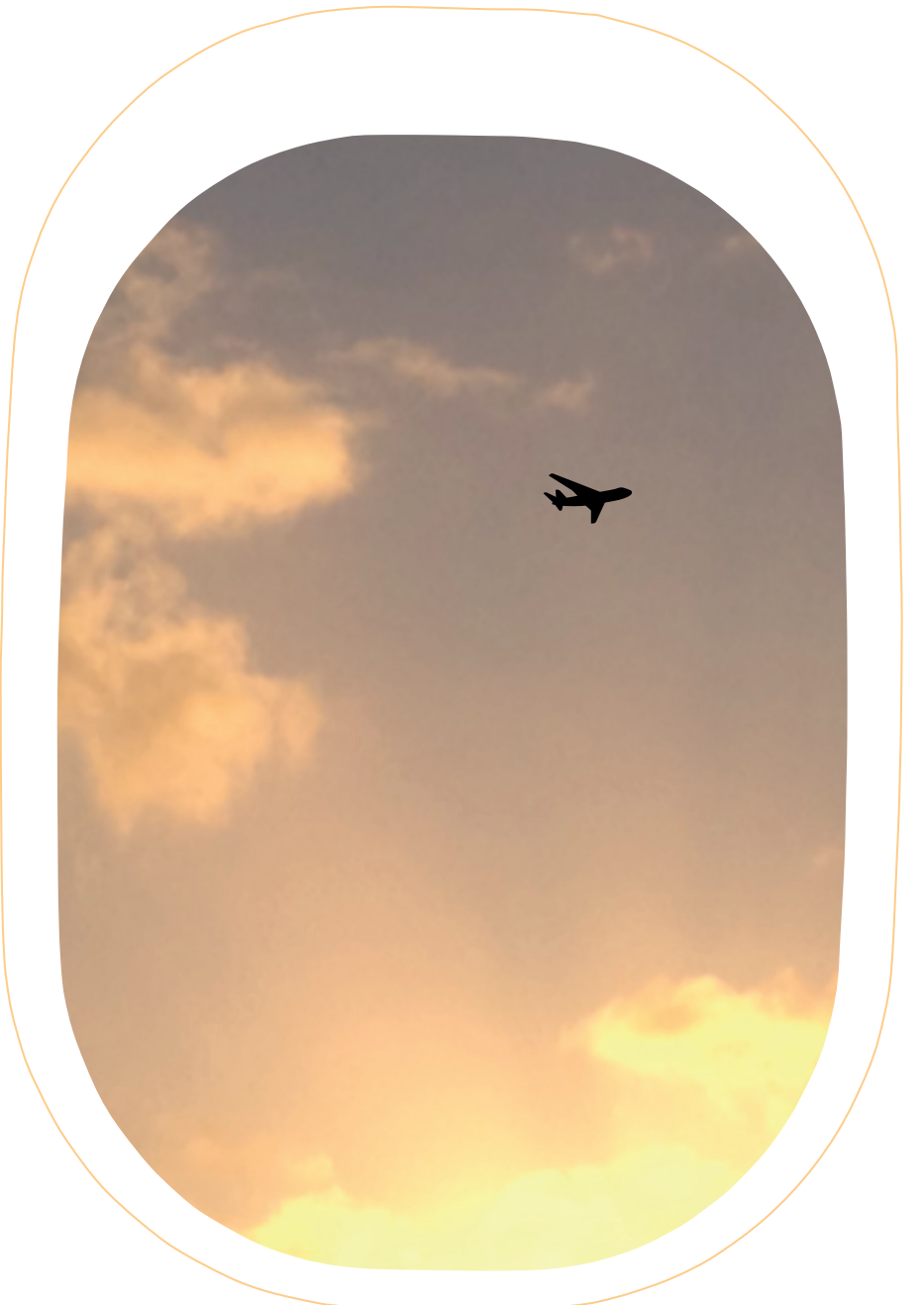
Hoofdstuk 4: Angstgevoeligheid (AS) had geen invloed op de relatie tussen zelfgerapporteerde somatische gewaarwordingen en vliegangst, dit mogelijk als gevolg van een plafondeffect. Fysiologische reactiviteit liet wel een interactie met AS zien: veranderingen in hartslagfrequentie en parasympathische reactiviteit tijdens werkelijke vluchten waren sterker geassocieerd met veranderingen in de mate van vliegangst van vóór de behandeling tot na de vlucht voor deelnemers met een hoge AS, en minder sterk voor deelnemers met een lage AS.

Hoofdstuk 5: Het in dit hoofdstuk beschreven onderzoek ging in op het gebruik van cognitieve copingstrategieën in relatie tot behandelingsresultaten op de lange termijn. Vliegangstige deelnemers lieten een klinisch significante verbetering zien in het gebruik van cognitieve copingstrategieën. Individuele verschillen in deze veranderingen waren indicatief voor vliegangst op de lange termijn en vlieggedrag tot drie jaar na afsluiten van de behandeling. Met name een afname van het gebruik van niet-adaptieve copingstrategieën was gerelateerd aan een beter behandelingsresultaat.

Hoofdstuk 6: Dit onderzoek behandelde de vraag of angstactivering en habituatie tijdens (in-vivo) exposure de therapieresultaten op korte en lange termijn kunnen voorspellen. Hogere niveaus van zelfgerapporteerde angst vlak voor in-vivo exposure, maar niet fysiologische indicatoren van angstactivatie vlak voor in-vivo exposure, waren gerelateerd aan minder goede behandelingsresultaten op de lange termijn. De mate van anticipatieangst vlak voor in-vivo exposure zou mogelijkerwijs een indicatie kunnen zijn van bereidheid én gereedheid voor die exposure. Te hoge anticipatieangst zou kunnen leiden tot experiëntiële vermijding waarbij de emotionele verwerking wordt belemmerd. Hartslag habituatie tijdens de eerste in-vivo vlucht en een verhoging van de parasympatische activiteit tijdens de tweede in-vivo vlucht voorspelden een vermindering van vliegangst op de korte termijn, maar niet van vliegangst drie jaar na het afronden van de therapie of vlieggedrag op de lange termijn. Hartritme was de enige fysiologische variabele die was gerelateerd aan het behandelingsresultaat op de lange termijn: een lagere hartritme-reactiviteit aan het einde van de in-vivo vluchten was gerelateerd aan minder vliegangst drie jaar na afronding van de behandeling.

Hoofdstuk 7: In dit hoofdstuk werd onderzocht of de responscoherentie (de gelijktijdige verandering van subjectieve en fysiologische reactiviteit) toenam met emotionele intensiteit. Daarnaast werd onderzocht of de sterkte van deze coherentie mogelijk een indicatie was van de voortgang tijdens de therapie. De resultaten lieten geen relatie zien tussen de intensiteit van de fobische stimuli en de omvang van de synchrone verandering in subjectieve en fysiologische reactiviteit. Ook vonden we geen ondersteuning voor het functionalistische standpunt dat succesvolle behandeling van angststoornissen wordt aangegeven door een synchrone verandering in emotie-responssystemen.

Hoofdstuk 8: Vliegangst is een heterogene stoornis met grote interindividuele verschillen in aanvang, duur, ernst van de symptomen en vooral co-morbiditeit met andere fobieën en angststoornissen. Het empirische onderzoek in dit proefschrift richtte zich op individuele verschillen in subjectieve en fysiologische reactiviteit op vlucht gerelateerde stimuli. De resultaten van deze studies zijn gemengd, waardoor het moeilijk is om ze in een bepaald theoretisch model in te passen. De relatie tussen emotie-responssystemen wordt waarschijnlijk beïnvloed door vele variabelen, inclusief hogere orde cognitieve processen. Individuele verschillen in subjectieve en fysiologische reactiviteit op vlucht gerelateerde stimuli vóór de behandeling, en het gebruik van adaptieve en niet-adaptieve cognitieve copingstrategieën vóór de behandeling waren niet voorspellend voor het klinische verloop na de behandeling op de korte en lange termijn. Gedurende de therapie werd de relatie tussen de individuele reactiviteit en de behandelingsresultaten sterker. De mate van verandering in het gebruik van niet-adaptieve copingstrategieën tijdens de therapie was indicatief voor het voortduren van vliegangst op de lange termijn en het aantal door deelnemers gemaakte vluchten binnen drie jaar na het afsluiten van de behandeling. Subjectieve reactiviteit vlak voor in-vivo exposure en tijdens in-vivo exposure was voorspellend voor de behandelingsresultaten op de korte en lange termijn. Het toevoegen van metingen van fysiologische reactiviteit verbeterde de voorspelling van de behandelingsresultaten. De omvang van de synchrone verandering in subjectieve en fysiologische reactiviteit nam niet toe bij een hogere intensiteit van fobische stimuli en was niet gerelateerd aan therapieresultaat. Subjectieve en fysiologische metingen van angstactivatie boden gedeeltelijk onafhankelijke informatie. Fysiologische metingen van angstactivatie zouden daarom kunnen bijdragen aan een betere voorspelbaarheid van therapieverloop en therapie-uitkomst.



Dankwoord

DANKWOORD

Hoewel je een proefschrift voornamelijk in je eentje schrijft, zijn er veel anderen bij betrokken. Ik gebruik deze mogelijkheid dan ook graag om iedereen te bedanken voor zijn of haar bijdrage.

Allereerst en allermeest gaat mijn dank uit naar alle deelnemers aan het onderzoek: de patiënten met vliegangst, die belangeloos participeerden. Bijzondere mensen, die ondanks de intensiteit van hun angst de confrontatie aangaan met die angst en zich aanmelden voor therapie. Stoer volk, dat tijdens intensieve therapie ook nog eens meedoet aan wetenschappelijk onderzoek waar ze zelf geen baat bij hebben. Ik zou jullie allemaal graag willen noemen hier, maar privacyoverwegingen beletten dat. Dank ook aan alle participanten zonder vliegangst. Hoofdstuk 2 en hoofdstuk 3 waren er niet geweest zonder jullie inzet.

Lucas, tijdens het varen door Friesland ter ere van jouw promotie hebben we voor het eerst gesproken over fysiologisch georiënteerd onderzoek bij mensen met vliegangst. Jij was vanaf het prille begin enthousiast. Binnen no time werd de geplande verbouwing van het mooie VALK-gebouw aangepast en was een 'plakkamer' gerealiseerd. Wat begon als idee voor wat kleine onderzoekjes werd al snel opgewaardeerd naar een volledig promotieonderzoek toen Philip langszij kwam als supervisor en promotor.

Philip, dank voor alle begeleiding. Dankzij jouw subtiele aanwijzingen is dit proefschrift gegroeid naar wat het nu is. Bij jou staat de inhoud altijd op de voorgrond. En ook al duurde het traject lang, je bleef enthousiast. Petje af dat je ondanks je drukke werkzaamheden als decaan van de Faculteit Sociale Wetenschappen toch nog tijd en energie had om snel te reageren op mijn mails.

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Dit onderzoek is een VALK onderzoek. Dank aan iedereen die daar rondliep en rondloopt. Om te beginnen dank aan de bestuursleden van stichting VALK voor het vertrouwen. Wetenschappelijk onderzoek in een therapeutische setting zorgt voor extra werk en extra druk op de uitvoering. Het organisatorische talent van het secretariaat speelde een grote rol in de vlekkeloze uitvoering. Goed gedaan Ans, Fiona, Willeke, Bep, Eline en alle stagiairs.

Zonder de welwillende en enthousiaste medewerking van alle psychotherapeuten was dit onderzoek niet gelukt. Lucas, Josine, Imke, Claudia, Marco, Marijke, Christelle, Sietske, bedankt. De praktische aspecten van psychofysiologisch onderzoek hebben het voor jullie niet gemakkelijker gemaakt. Groepstherapie is een sport op zich, om dan ook nog eens de extra belasting te hebben van een psycholoot die jullie protocol ontregelt, maakt het topsport. Extra hulde voor de kanjers van therapeuten die telkens twee volle dagen groepstherapie wisten te combineren met de belasting van het uitvoeren van psychofysiologisch onderzoek.

Dank ook aan alle VALK-vliegers: Ronald, René, Hadewey, Frank, Frank, Thijs, Eric, Mark, Maarten, Andries. De invloed van de vliegers op het therapieresultaat is groter dan jullie wellicht denken. Jullie hulp bij het uitvoeren van het onderzoeksprotocol (bijhouden wanneer wat) heeft de kwaliteit van de dataverwerking verhoogd.

Veel dank ben ik verschuldigd aan de onderzoekstagiairs: Fiona, Katerina en Helene. Zonder jullie hulp waren de metingen niet uitgevoerd, de meetfiles niet gelabeld en de datafiles niet gevuld. Ad wil ik bedanken voor de anamnese van alle participanten zonder vliegangst. Safiyeh voor de data-acquisitie van de 3-jaar-follow-up.

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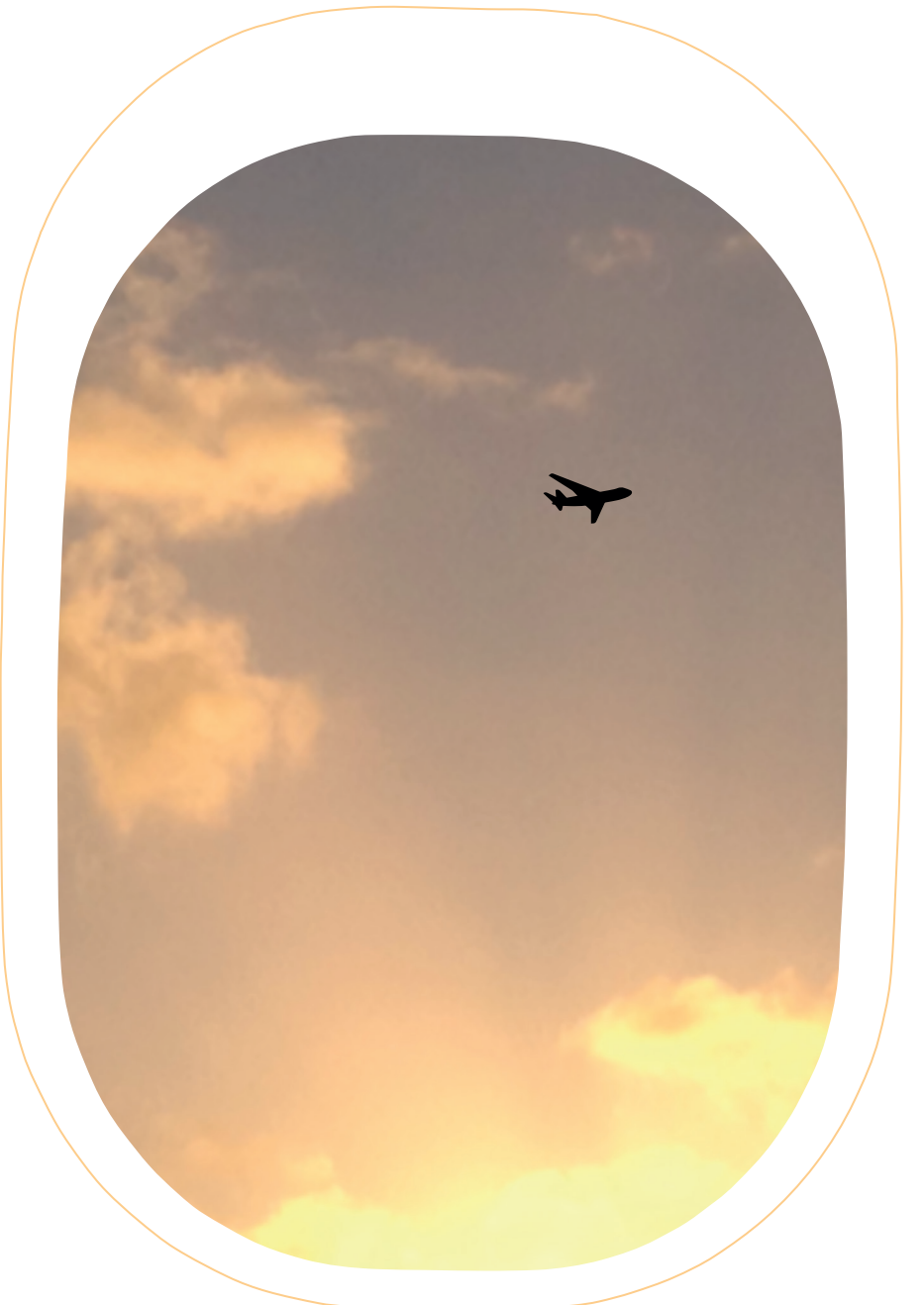
Jos, dank voor het beschikbaar stellen van de VU-AMS apparatuur en de inspirerende gesprekken. Piekeren is zeker een component die bijdraagt aan vliegangst en meer onderzoek rechtvaardigt. Ook bedank ik Esther voor het mooie ontwerp van dit boekje.

Ten slotte, niets zo belangrijk als mijn gezin. Wat een genot om door je kinderen op de hak te worden genomen. Martijn, Myrthe en Lisabelle, door jullie relativerende opmerkingen werd alles weer in perspectief gezet, heerlijk. Hoe mooi om te zien dat onze dochters Myrthe en Lisabelle nu naast me staan als paranimfen. Tim en Martijn, dank voor het constructieve commentaar.

Else, mijn grote liefde, zonder jou was dit project al meermalen gestrand. Tijdens de rust van onze wandelingen hielp je structuur aan te brengen door te vragen om verduidelijking. En als ik er de brui aan wilde geven, wist jij me af te houden van overhaaste acties. Deze dissertatie is ook jouw dissertatie.



Curriculum vitae

CURRICULUM VITAE

Bert Busscher is geboren op 30 november 1959 in Delfzijl en voltooide in 1979 het VWO in Appingedam. Dat jaar startte hij met de opleiding tot verkeersvlieger aan de RLS in Eelde. Hierna volgde een jaar studie in de ergonomie en human factors aan de University of Technology in Loughborough, UK. Sinds 1983 is Bert werkzaam bij de KLM als verkeersvlieger. Hij werkte als instructeur en auditor en heeft ruim 28 jaar ervaring als gezagvoerder, sinds 2001 tot heden op de Boeing 747. In 1998 studeerde hij af in de psychologie aan de Universiteit van Amsterdam, met als afstudeerrichting psychonomie. Sinds 2010 staat Bert geregistreerd als luchtvaartpsycholoog bij de European Association for Aviation-Psychology (EAAP). Tijdens zijn werkzaamheden als vrijwilliger bij Stichting VALK startte hij met wetenschappelijk onderzoek naar diverse aspecten van vliegangst, hetgeen resulteerde in dit proefschrift.