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SCREENING AND MITIGATION OF ANXIETY IN UNIQUE ENVIRONMENTS

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SCREENING AND MITIGATION OF ANXIETY IN UNIQUE ENVIRONMENTS

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SCREENING AND MITIGATION OF ANXIETY IN UNIQUE ENVIRONMENTS

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Anxiety and other psychological conditions may present challenges for commercial spaceflight operations, as little is known regarding the psychological effects of spaceflight on laypersons. A recent investigation evaluated measures of anxiety during centrifuge-simulated suborbital commercial spaceflight, highlighting the potential for severe anxiousness to interrupt spaceflight operations. To pave the way for future research, an extensive literature review identified existing knowledge that may contribute to formation of interventions for anxiety in commercial spaceflight. Useful literature was identified regarding anxiety from a variety of fields, including centrifugation, fear of flying, motion sickness, and military operations. Fear of flying is the most extensively studied area, with some supportive evidence from centrifugation studies. Virtual reality exposure (VRE) is as effective as actual training flight exposure (or analog exposure) in mitigation of flight-related anxiety. The addition of other modalities, such as cognitive behavioral therapy or biofeedback, to VRE improves desensitization compared to VRE alone. Motion-sickness susceptible individuals demonstrate higher trait anxiety than non-susceptible individuals; for this reason, motion sickness susceptibility questionnaires may be useful measures to identify at-risk individuals. Some military studies indicate that psychiatric history and personality classification may have predictive value in future research. Medication countermeasures consisting of benzodiazepines may quell in-flight anxiety, but do not likely improve anxiety on repeat exposure. The scarce available literature addressing anxiety in unique environments indicates that training/repeated exposure may mitigate anxiety. Anxiety and personality indices may be helpful screening tools, while benzodiazepines may be useful countermeasures when needed.

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List of Abbreviations

16PF	16 Personality Factors test
BDU	Battle Dress Uniforms
BZD	Benzodiazepine
CBT	Cognitive Behavioral Therapy
FOF	Fear of Flying
GI	Guided Imagery
HRV	Heart Rate Variability
IPAT	Institute for Personality and Ability Testing Anxiety Scale
MMPI	Minnesota Multiphasic Personality Inventory
MOPP	Mission Oriented Protective Posture
MSS	Motion Sickness Susceptibility
MSSQ	Motion Sickness Susceptibility Questionnaire
MT	Music Therapy
NEO-PI-3	NEO Personality Inventory-3
SAI	State Anxiety Inventory
SE	Standard Exposure
SFP	Spaceflight Participant
SRSI	Smith Relaxation States Inventory
STAI	State-Trait Anxiety Inventory
UMACL	University of Wales Institute of Science and Technology Mood Adjective Check List

VRE	Virtual Reality Exposure

Chapter 1: Introduction

Anxiety and other psychological conditions may present challenges for commercial spaceflight operations, particularly as little is known regarding the psychological effects of commercial spaceflight on participants. A recent investigation identified anxiety and stress during centrifuge-simulated suborbital commercial spaceflight, and highlighted the potential for severe anxiousness to interrupt spaceflight operations [1]. Research is needed to better assess the feasibility and utility of screening and mitigation tools for anxiety during commercial spaceflight operations. To pave the way for such work, an extensive literature review was performed in order to identify existing knowledge that may contribute to formation of interventions for anxiety during commercial spaceflight.

Most of the psychological knowledge regarding humans in spaceflight is based upon studies of career astronauts selected under stringent medical and psychological standards. Although there is limited information regarding the tolerance of commercial spaceflight participants (SFPs) with chronic medical conditions to spacecraft acceleration profiles, there has been little research into anxiety and psychological concerns as they relate to commercial spaceflight [2–4]. Unlike career astronauts, SFPs are unlikely to undertake a prolonged ground-training curriculum prior to launch, potentially leaving them unprepared for the psychological stressors of commercial spaceflight.

Human centrifuge training has been utilized extensively for the training of career astronauts, and could be used to prepare SFPs for the experience of commercial spaceflight. Centrifugation may offer the first chance to observe future SFPs in a high-stress analog environment that may elicit similar anxiety responses to those that could occur during spaceflight. A recent investigation utilized centrifuge-simulated suborbital spaceflight to study anxiety in potential commercial SFPs [1]. In this study, twelve of the 86 subjects (14%) experienced some degree of anxiety that interfered with their ability to complete the centrifuge training [1]. Positive psychiatric history and self-reported symptoms did not predict anxiety during centrifuge performance [1]. No specific intervention strategies were attempted, but 9 of the 12 participants with anxiousness were able to complete their centrifuge run after coaching and support from study facilitators [1]. Apart from this study, little research has evaluated psychological considerations for suborbital spaceflight.

Given the potentially severe implications of anxiety during commercial spaceflight operations, additional inquiry into this topic is critical. This manuscript will review available literature pertaining to the concern for anxiety in commercial spaceflight activities and similar analogue environments, in particular focusing on identification techniques and mitigation strategies such as exposure therapy, cognitive behavioral therapy, and relaxation techniques. The application of such techniques for future short-duration commercial spaceflight activities will be discussed, as well as areas requiring further research.

Chapter 2: Methods

A systematic literature review of currently available information was undertaken utilizing PubMed, Google Scholar, and the Defense Technical Information Center to identify useful literature regarding anxiety in commercial aviation, spaceflight, and appropriate analogues. This effort examined a variety of related fields, such as centrifugation, fear of flying (FOF), motion sickness, military protective gear, submarine, and polar operations. Search terms included "anxiety," "anxiousness," "psychological," "psychiatric," "centrifuge," "centrifugation," "fear of flying," "motion sickness," "military," "submarine," "polar," "Antarctica," "benzodiazepines," and "memory impairment." Titles obtained from these criteria were reviewed for relevancy.

Articles published in a language other than English without an available translation and articles not involving human subjects were rejected. All other relevant documents including the search terms noted above were reviewed in their entirety. Furthermore, the references of these studies were examined to identify further applicable work. Using this strategy, 34 studies were identified that met the search criteria and were deemed relevant to this topic. Seven studies examined benzodiazepines (BZDs) that were either not commonly utilized today or unfeasible for commercial spaceflight use, due to side effects, route of administration, and inappropriate levels of sedation, and were excluded. Four of the studies addressed only non-acute exotic situations (e.g. long-duration Antarctic missions) and were excluded as they do not appear to pertain to short-duration commercial spaceflight activities. One study provided only speculation regarding sensorimotor adaptation for spaceflight and was excluded. The remaining 22 investigations were included in this review. Of note, several of the studies are non-peer-reviewed technical reports from military data; they are included here due to the lack of other, peer-reviewed sources available for study.

Chapter 3: Results

Because commercial spaceflight literature is very limited at present, this review focuses on research performed primarily in analogue environments. Despite intrinsic differences from the spaceflight setting, FOF and centrifugation represent the closest equivalents to our intended environment in the available literature. The majority of the works identified for this review fall into the FOF realm, with a smaller proportion of articles addressing centrifugation and military analogues. Studies addressing the link between motion sickness and anxiety or personality factors were also identified as pertinent, as were investigations which examined the use of benzodiazepines for equivalent situations. The information from each of these areas will be presented in corresponding subsections below.

FEAR OF FLYING

With regards to anxiety in unique and extreme environments, most prior investigation has focused on FOF. This literature has often concentrated on comparison of mitigation strategies such as exposure therapy via actual training flights or virtual reality paired with psychological therapy, including cognitive behavioral therapy or relaxation techniques [5–7]. Prior research in this area has had far-reaching benefit among the public as anxiety in the flight environment or within enclosed spaces is fairly prevalent, with up to 20% of the general population estimated to suffer from some degree of FOF [5,8,9].

The main treatment options available for FOF are standard exposure (SE) or virtual-reality exposure (VRE) therapies. SE generally involves ground-based airplane exposure while VRE utilizes a computer to simulate the aircraft environment. Adjunct therapy such as cognitive behavioral therapy (CBT) or relaxation therapy has also been examined. Most sources identify VRE as particularly useful for the treatment of numerous phobias, though mixed results have been noted [10]. In a meta-analysis of 49 articles regarding FOF treatment, VRE alone was noted to be an effective treatment for fear of flying [5]. In addition, VRE plus CBT has been demonstrated to be more effective than CBT alone [10]. Patients receiving a combination of VRE with CBT or relaxation techniques have demonstrated reduced fear or anxiety associated with flying [5]. VRE has also been noted to be superior to imaginal exposure (subject to mentally visualizes a fear-inducing situation) and bibliotherapy (provision of a book on FOF with encouragement to read about their condition), though VRE with biofeedback is generally superior to VRE alone [10].

In comparison, prior research has attempted to identify the length of SE therapy required to elicit an improvement in symptomology. For example, one study examined one- versus five-session SE therapy (involving in vivo flight exposure) and cognitive restructuring, where a single session consisted of three hours of treatment and a five session series consisted of a total of six hours of gradual treatment [11]. There was no significant difference between the two treatment groups, and both were relatively successful in improvement of FOF symptoms during a behavioral test flight [11]. However, at one-year follow-up, there was a significant ($p<0.05$) decrease in the number of steps completed in the behavioral test flight for the single-session group, and a similar marginal decrease in the five-session group ($p<0.08$), demonstrating a high degree of relapse in both groups [11].

Another study compared SE to VRE to identify relative benefits and success in mitigation of flight-related anxiety [6]. In this study, subjects with known DSM-IV diagnoses of flight-related specific situational phobia or panic disorder with agoraphobia underwent 6 weeks of treatment with either VRE or SE [6]. Subjects were evaluated by measures including the Fear of Flying Inventory [12], the Questionnaire on Attitudes Toward Flying [13], and the Client Satisfaction Questionnaire–8 [14]. Participants in both the VRE and SE groups were highly satisfied with the treatment they received, and both VRE and SE were demonstrated to be effective based on standardized questionnaires, self-rated improvements, satisfaction scales, and number of participants who actually flew after treatment [6]. These findings support the use of VRE as a reasonable alternative to SE for the treatment of FOF.

Several investigations have examined the efficacy of VRE in comparison to other psychological techniques. Krijin et al compared the treatment of FOF with VRE to CBT and bibliotherapy (provision of a book on FOF with encouragement to read about their condition) [7]. The subjects in this study with divided between VRE, CBT, and bibliotherapy groups; those in the bibliotherapy group were then randomized to VRE or CBT after 5 weeks and interim testing [7]. When comparing the initial groups, a significant decrease in the anxiety was reported on questionnaires from subjects in the VRE and CBT groups compared to the bibliotherapy group [7]. After both the VRE and CBT groups underwent the addition of group CBT, there was further decline in anxiety [7]. In this study, comparison of VRE or CBT alone was not made to combination CBT-VRE.

Another study by Wiederhold et al evaluated the utility of biofeedback in combination with VRE [15]. Biofeedback in the form of heart rate, respiratory rate, skin resistance, and skin temperature was employed. The 36 phobic patients were trained in diaphragmatic breathing skills with the use of visual feedback for heart and respiratory rates; after treatment, 33 of the phobic subjects were able to complete a behavioral test flight [15]. In their early sessions, these successful subjects were noted to have heightened physiologic arousal, measured by skin resistance, that did not return to baseline by the end of the session [15]. However, throughout the course of treatment these participants demonstrated a gradual trend toward the non-phobic levels of arousal, demonstrating success of the combined VRE and biofeedback techniques [15]. In contrast, the three phobics who were unsuccessful in completing a behavioral test flight demonstrated erratic physiological arousal patterns and did not trend toward the non-phobic response by the final training session [15].

An additional investigation assessed the longer-term efficacy of VRE, biofeedback, and imaginal exposure [16]. The initial study consisted of three groups with ten participants in each: VRE with biofeedback, VRE alone, and imaginal exposure alone [16]. At the conclusion of the initial investigation, 100% of the subjects in the VRE with biofeedback group completed a behavioral test flight, where only 80% of the VRE alone group and 10% of the imaginal exposure alone group successfully completed behavioral test flights [16]. The investigators then contacted the participants three years later to evaluate maintenance of treatment effect: three years post-treatment, all of the VRE with biofeedback group maintained the ability to fly, demonstrating sustained high-effectiveness of this treatment combination, while 2 of VRE alone group were no longer able to fly [16]. The one participant in the imaginal exposure group who was able to fly at the end of treatment continued to do so [16]. Of note, numerous participants reported that the skills provided during treatment had been generalized into everyday stress management techniques; similarly, one subject reported utilizing the techniques he learned during the study to conquer his fear of heights without the assistance of a therapist [16]. For perspective, it is interesting to note that these follow-up interviews took place in January 2002, which were several months after the September 11, 2001 terrorist attacks. Despite the general fear concerning flying at that time, these subjects maintained the successful effects of their treatment.

Mühlberger et al also evaluated VRE for treatment of FOF [17]. However, in contrast to other investigations, the groups in this study were differentiated based upon whether a therapist accompanied each subject on their graduation flight or whether the subject took this flight alone, attempting to evaluate the benefit of provider presence [17]. Training consisted of four VRE flights completed in one session, after which participants completed a graduation flight either alone or with a group of other participants and a therapist [17]. A significant reduction in FOF was noted after treatment, regardless of treatment group; overall, 67% of unaccompanied and 87% of accompanied subjects completed their graduation flight, though this was a non-significant difference [17].

CENTRIFUGATION

In contrast to the more copious literature available regarding FOF, there is less information available to address the subject of anxiety or mood during centrifugation. Of the few existing studies, only two specifically addresses the psychological effects of +Gz centrifugation [18,19]. One study utilized the University of Wales Institute of Science and Technology Mood Adjective Check List (UMACL) to evaluated energetic arousal, tense arousal, and hedonic tone in 19 Polish male cadets [18]. As energetic arousal has been associated with better performance of vigorous actions, the authors attempted to identify where the cadets might receive the benefit of such arousal as opposed to deleterious effects of tense arousal and anxiety. In this study, centrifuge runs started at +3 Gz and increased incrementally until peripheral light loss (tunnel vision) occurred [18]. Based on the UMACL, energetic arousal was lowest 2 hours pre-centrifugation and rose then remained stable, while tense arousal rose sharply to its highest level at 2 minutes pre-centrifugation [18]. However, centrifugation apparently had a positive impact on subject arousal and anxiety state, as tense arousal dropped below the baseline value post-centrifugation, suggesting that the experience itself worked to decrease subject anxiety state [18].

The other centrifuge investigation compared the efficacy of guided imagery (GI) to music therapy (MT) for reduction of anxiety during centrifugation in 12 subjects [19]. Anxiety was quantified via the Smith Relaxation States Inventory (SRSI), State Anxiety Inventory (SAI), heart rate, maximum heart rate, and heart rate variability (HRV) [19]. Prior to centrifugation, a baseline heart rate was obtained and the subjects completed baseline a SRSI and SAI; afterwards, the GI group received 15 minutes of GI instructions via voice recording while the MT group received 15 minutes of light music [19]. The results were notable for significantly decreased state anxiety post-intervention but pre-spin in the GI group compared to the MT group and lower maximal heart rate in the GI group, suggesting that GI may decrease sympathetic arousal (and resultant potential for anxiety) during centrifugation [19].

MOTION SICKNESS

Because there is concern that motion sickness or other somatic sensations experienced during centrifugation or suborbital spaceflight may contribute to anxiety in participants, and that those susceptible to motion sickness may also be susceptible to related anxiety, the available literature regarding motion sickness was reviewed for relevant information. In one study, Collins and Lentz examined the correlation between personality and motion sickness [20]. Motion sickness susceptibility was stratified by a motion sickness questionnaire and the subjects were divided into four groups of 37 subjects each (highly susceptible men, highly susceptible women, non-susceptible men, non-susceptible women) [20]. Each subject underwent a battery of tests. On the State-Trait Anxiety Inventory, notable findings include higher trait anxiety scores in susceptible vs non-susceptible individuals regardless of sex [20]. State anxiety was similar prior to rotary vestibular stimulation, but was significantly higher in susceptible individuals after rotation [20]. On the Eysenek Personality Inventory, non-susceptible individuals had significantly higher scores on the extraversion scale while susceptible individuals had significantly higher scores on the neuroticism scale [20]. On the 16 Personality Factors test (16PF), non-susceptible individuals tended to score as less neurotic, better adjusted, and more venturesome; in contrast, susceptible individuals were generally more tenderminded and subjective [20].

Another study by Lentz and Collins further examined the characteristics related to motion sickness susceptibility by evaluating 2,432 undergraduate students in local universities who completed several motion sickness questionnaires along with biographic data [21]. The authors noted that more women than men reported motion sickness and that highly motion susceptible individuals did not enjoy movies with emphasis on rapid action [21].

Fox and Arnon investigated the connection between motion sickness and anxiety in 94 Israeli fighter pilot cadets [22]. Each pilot completed numerous anxiety questionnaires including the State-Trait Anxiety Inventory, Taylor Manifest Anxiety Scale, Eysenck Personality Questionnaire, and 16PF, then undertook five light airplane flights over the course of a week [22]. In these subjects, nausea was the most commonly self-reported symptom (46% of subjects) and nausea and sweating were the most commonly instructor-identified symptoms (17% and 19%, respectively) [22]. While there was no significant correlation between the self- and instructor-reported symptoms, anxiety scores were correlated with self-reported motion sickness (but not instructor-observed) [22].

Paillard et al examined the link between anxiety and motion sickness susceptibility [23]. The study included 167 healthy subjects and 94 subjects with a variety of chronic vestibulopathies, and each subject completed a Motion Sickness Susceptibility Questionnaire (MSSQ) and a Trait Anxiety Questionnaire [23]. When the subjects with vestibulopathies were separated into those with and without vestibular loss, those with vestibular loss had lower MSSQ scores than healthy subjects, who in turn had lower MSSQ scores than vestibulopathic patients without vestibular loss [23]. These differences were not accounted for by sex, age, trait-anxiety, or interaction, though the authors found that women reported higher MSS than men and that MSS declined with age [23]. However, the relationship between anxiety and MSS scores was weak and only significant in healthy subjects [23].

While identifying and characterizing motion sickness and the neurovestibular alterations resulting from suborbital spaceflight may be useful, management of these considerations is important as well. These issues have received some attention. A suborbital spaceflight is likely to last approximately 2-3 hours, with around 3-6 minutes of microgravity. Karmali and Shelhamer suggest that 3-4 minutes of microgravity is insufficient for adaptation to occur during a suborbital spaceflight alone [24]. Because of this, the authors recommend pre-adaptation via parabolic flight to preemptively control for motion sickness symptoms in commercial SFPs [24]. The authors do note that research has identified some limitations in the transfer of adaptation from parabolic flight to orbital spaceflight, but given that the path for a suborbital spaceflight is effectively a large parabola, they suggest that adaptation may transfer to suborbital spaceflight more readily [24].

MILITARY

Several studies in the military literature have examined the effects of various aspects of anxiety in the military environment. These generally involve subjects placed in stressful training situations, many of which could be considered analogous to commercial spaceflight activities. For example, Warren et al examined the responses of subjects to training in Mission Oriented Protective Posture (MOPP) gear [25]. MOPP4 equipment offers the highest level of protection, and is designed to protect military personnel from a toxic environment (i.e. chemical, biological, radiological, or nuclear strike), by incorporating a respirator, rubberized boots, gloves, and a standard over garment [25]. Such occlusive gear is readily comparable to pressure garments that may be required for SFPs in commercial spaceflight activities. In this study, 12 male soldiers specializing as field engineers donned MOPP4 gear for two five-day periods while performing a variety of tasks [25]. For one five-day period, MOPP4 equipment was donned for the entirety of each study day; for the other period, Battle Dress Uniforms (BDU) were worn for the first four days followed by MOPP4 gear for the fifth day [25]. The State-Trait Anxiety Inventory was utilized to quantify anxiety, where trait anxiety was measured on the first day and state anxiety was recorded at the beginning of each day [25]. Additionally, participants completed the 16PF to assess personality [25]. The results were notable for increased state anxiety on the first day of donning MOPP4 gear; this effect diminished to baseline by the fifth day [25]. Interestingly, participants with high state anxiety before or after the test day also demonstrated characteristics of introversion on the 16PF, while subjects with low state anxiety displayed extraverted characteristics, suggesting that personality affects propensity towards anxiety in such situations [25].

In another study, Tharion et al examined the performance of subjects in a simulated chemical warfare environment, wearing MOPP4 gear, in correlation with personality factors [26]. A battery of tests including personality inventories and the State Anxiety questionnaire were administered prior to the start of the field exercise, every six hours during the field operation, and at completion [26]. "Casualties" (participants who withdrew voluntarily or were removed by medical monitors during testing) tended to exhibit greater depressive tendencies and lower self-motivation than "survivors" (the remaining participants who did not withdraw). State anxiety was significantly higher in "casualties" than "survivors" [26]. This suggests that personality, particularly of motivation and anxiety, may affect operational performance in occlusive gear.

As with occlusive garments, occlusive spaces, such as submarines, can elicit stress reactions and anxiety. A review of studies in such environments can be useful as analogs for spaceflight, particularly as they involve a potentially claustrophobic situation not without risk. In one such study, van Wijk examined the characteristics of 23 South African Navy student submariners and their responses during 3 days of submarine escape training [27]. This investigation obtained the State-Trait Anxiety Inventory and the Institute for Personality and Ability Testing (IPAT) Anxiety Scale measures pre- and post-training and indicated a significant decrease from training in both the covert and overt anxiety dimensions identified by IPAT [27]. On STAI, both subscales demonstrated decreased anxiety, but only the trait scale was statistically significant [27]. This study suggests that effective familiarization and training in the operational environment may improve an anxiety response over time.

MEDICATION

Should screening and exposure desensitization therapy not adequately mitigate the risk of anxiety during commercial spaceflight, other measures may be needed. Medication may play a role in both prophylaxis and treatment of anxiety in this unique environment, and the use of medication to mitigate anxiety is being considered by many industry participants. The main class of drug utilized in this role would likely be the BZDs, due to their demonstrated effectiveness in anxiety mitigation. However, the use of such medications raises concern, as appropriate therapy would need to balance effective extinguishment of anxiety with minimization of memory and operational impairment.

It is thought that the anterograde amnestic effect of BZDs is due to impairment of memory consolidation rather than a deficit in short-term memory [28]. Per Chouinard et al, the effect of BZDs on memory include impairment of delayed recall of word lists, while immediate recall is unaffected [29]. This appears to indicate some serviceable level of immediate physical and mental functionality of medicated individuals, even though the events may not later be possible to recall. With regards to the variability of memory impairment between different BZDs, the authors make note of several important principles. BZDs with higher lipid solubility, including alprazolam, diazepam, lorazepam, and trazolam, generally cause more severe amnesia, and BZDs with high affinity for the BZD receptor generally produce more severe memory impairment [29]. BZDs with short-to-intermediate half-lives also have more potential to cause amnesia [29]. Of the medications listed, lorazepam and triazolam are the most often associated with greatest memory loss [29]. Of note, tolerance to the memory impairment effects of BZDs occurs with chronic use and, once this has developed, the effects on memory are generally confined to the first 90 minutes of each dose.

In contrast to treatment with BZDs during in-vivo spaceflight, the use of these medications during training is questionable. Wilhelm et al examined the effects of BZDs during exposure therapy for FOF in 28 women, where each participant flew twice within a one week interval [30]. Prior to the flights, each participant received either placebo or 1mg of alprazolam, and they received the opposite medication for their second flight [30]. During the first flight, alprazolam reduced self-reported anxiety and symptoms more than placebo; however, an increase in heart and respiratory rate among the alprazolam on flight 1 group was noted during this flight, suggesting anxiety despite subject denial [30]. On the second (placebo) flight, this group reported more anxiety and a substantial increase in panic attacks than the placebo group on flight 1 [30]. The flight 1 placebo group demonstrated a decrease in self-reported anxiety during flight 2, and reported less anxiety than the flight 1 alprazolam group [30]. These findings support the articles previously discussed in the FOF section with regards to fear extinction via exposure. Unfortunately, this effect appears to be eliminated with use of BZDs during exposure therapy, as those subjects receiving BZDs during their initial flight demonstrated no benefit from repeat exposure to the flight environment once the BZD had been discontinued [30].

Further demonstrating the inefficacy of BZDs with exposure therapy, Coldwell et al investigated whether BZDs could facilitate desensitization to dental injection phobia [31]. 144 subjects with dental injection phobia underwent exposure therapy in concert with placebo or alprazolam [31]. The groups progressed through training at the same rate, and there was no difference between the groups on a post-treatment behavioral avoidance test [31]. Additionally, one year after study completion, fear of dental injection remained reduced similarly among the groups [31]. While a far cry from the flight environment, this study similarly demonstrated that use of BZDs during exposure therapy does not appear to contribute to desensitization.

Chapter 4: Discussion

Although there is limited literature addressing these specific topics in any one field, information can be gleaned from the studies presented for application within the spaceflight environment. For example, VRE and SE have been demonstrated to be equally effective as treatment for FOF. This finding suggests that centrifuge VRE (simulating suborbital spaceflight in a centrifuge, as performed in previous studies [1,3,4]for commercial SFPs may be an effective mechanism in the mitigation of anxiety and the preparation of SFPs for the actual spaceflight. The use of SE could be better evaluated for analogue environments, such as parabolic flight, which, as discussed above, has been suggested as a possible method for adapting SFPs to the vestibuloocular effects of spaceflight. However, given that VRE is more accessible, controlled, and economically palatable than SE (especially when considering the cost and impracticality of exposure to in-vivo commercial spaceflight), its use for desensitization of anxious commercial SFPs would likely be preferential, assuming that similar results to those found in FOF treatment could be obtained. Furthermore, the combination of VRE with additional modalities, such as CBT, may improve outcomes. Evidence demonstrates that biofeedback may also complement VRE as a form of anxiety mitigation. Interestingly, the skills learned during biofeedback therapy (e.g. diaphragmatic breathing) can be utilized successfully in other aspects of life, as reported above. Thus, SFPs that have undergone biofeedback training for other anxiety-related problems may be able to utilize this training for application within the spaceflight environment.

VRE is significantly more effective than imaginal exposure, indicating that desensitization methods utilizing sensory stimulus are more likely to be successful than simply asking participants to visualize their own future flight. The limitations of VRE likely stem from the inability of some subjects to achieve suspension of disbelief and elicit anxiety during the sessions; unfortunately, this may make VRE an ineffective treatment for some. Based on the literature examined, combination treatment of FOF with VRE and CBT or relaxation techniques appears to be quite effective. The addition of CBT or relaxation techniques to VRE via centrifuge may improve outcomes in those with fear of spaceflight. Of note, it appears that therapist accompaniment during exposure is not particularly useful; this finding argues against the inclusion of a therapist for training on a spaceflight with a concerning participant at high risk for anxiety-related reactions. Finally, while FOF is the best-studied of the subjects examined in this review, additional research would be useful for comparison of the varying types of adjunctive therapy (i.e. CBT, biofeedback, relaxation) when paired with VRE, particularly if such studies could be undertaken to examine specifically the spaceflight environment (or close analogues).

Similar, albeit more limited, findings were identified in the centrifuge literature as well. Guided imagery appears to reduce stress prior to centrifugation. This effect may be useful during centrifugation training and potentially in suborbital spaceflight applications as well. In terms of quantification of anxiety, one of the studies demonstrated that centrifugation increases energetic arousal (a positive change), and that tense arousal peaked immediately prior to centrifugation and slumped below baseline levels afterward (again, an improvement); the UMACL tool utilized by this study may be a useful rapid measure to obtain for future centrifugation studies examining anxiety and training response [18].

The correlation of motion sickness and personality traits was examined in several investigations, with the general consensus suggesting that higher trait anxiety may be correlated with high risk of motion sickness susceptibility. While some of the personality measures applied in this older research are not as widely used today, the differences noted on these tests indicate the possible utility of personality testing for motion sickness susceptibility screening, or vice-versa. Personality indices that include an anxiety component such as Minnesota Multiphasic Personality Inventory (MMPI) or NEO Personality Inventory-3 (NEO-PI-3) may be useful in screening for individuals likely to experience anxiety in certain situations. Some studies have demonstrated that anxiety correlates with self-reported motion sickness symptoms but not objectively identified cues (such as instructor-reported symptoms); this may result from a reciprocal effect of anxiety on motion sickness and vice-versa. Alternatively, this may also be a result of the difficulty in the objective identification of anxiety by an outside observer, especially when tasked with other duties while acting as an instructor pilot. Other research has indicated that the vestibular system is heavily involved in motion sickness susceptibility. While trait anxiety may play a role in motion sickness susceptibility, this appears to only be true in healthy subjects. It is important to note that the relationship between personality traits and motion sickness has been studied in Earth-bound environments. This relationship has yet to be characterized with space motion sickness as there is little data available. Even so, the MSSQ will likely be a useful measure to collect for comparison with anxiety measures.

Military literature involving chemical warfare protective garments and submarine escape training indicates that psychiatric history (anxiety, depression, etc), the STAI, and personality indices (to assess extroversion/introversion) may be useful screens for individuals likely to experience anxiety in unique and stressful situations, again potentially applicable to the spaceflight environment. These studies also indicate that desensitization therapy effectively mitigates anxiety caused by chemical protective gear. These findings are similar to those for FOF and support the use of training in as close an analogue to the operational environment as possible for an effective management strategy for situational anxiety. Furthermore, assessment for correlation between personality traits (in this case, introversion vs extroversion) may identify SFPs at risk for anxiety.

In the cases of failed identification or mitigation of anxiety in these unique environments, short- or long-acting BZDs can play an important role in achieving acute anxiolysis. Most literature on anxiolytics focuses on other aspects such as efficacy or pharmacokinetics; little focus given to memory impairment and little information is available. Studies have demonstrated that BZDs with high lipid solubility, high affinity for the BZD receptor, and short-to-intermediate half-lives generally produce more amnesia; given the tourist and experiential nature of commercial spaceflight, amnesia would not be an acceptable side effect. In the case of a commercial SFP whose anxiety remains uncontrolled after exposure therapy, prophylaxis with longer-acting, less lipophilic BZDs such as clonazepam or possibly alprazolam may mitigate anxiety while limiting memory impairment and allowing improved recall of the spaceflight at a later date. However, BZD use has been demonstrated to impair fear extinction during exposure therapy. As such, BZDs should not be employed during exposure training if the goal is fear extinction as this response is inhibited by BZDs and would negate the benefits of training. Finally, it would be preferable to expose individuals that may need BZD pharmacologic intervention to medications prior to use during the spaceflight experience in order to familiarize them with medication effects, note any unwanted side effects, and potentially limit the acute amnestic responses.

There are many limitations to the studies presented in this review. It is important to note the paucity of information available addressing the subjects discussed in this review. Even in FOF, which is better studied than other fields, much remains unknown. Furthermore, it should be mentioned that much of the research examined in this review suffers from small sample sizes, and therefore its application to the population at large may be limited. There are large gaps to our understanding of anxiety and the response of laypersons to the commercial spaceflight environment, and significant research should be undertaken to identify potential anxiety triggers, mitigation strategies, and those at the greatest risk.

Even so, this literature review has identified several important facts with regards to anxiety in unique environments such as spaceflight. In particular, the combination of VRE with other strategies such as CBT, relaxation therapy, or biofeedback may be ideal for effective anxiety mitigation prior to a commercial spaceflight. Military studies suggest that a careful psychiatric history (particularly regarding anxiety, depression, and similar psychological disorders), the State-Trait Anxiety Inventory, and personality indices (to assess extroversion/introversion) may be useful screens for spaceflight-related anxiety studies. Furthermore, personality indices that include a measurement of anxiety such as the MMPI or NEO-PI-3 may be useful in screening for individuals likely to experience anxiety in certain, high-stress situations. In the case that VRE, CBT, or other strategies fail to mitigate anxiety, or that a propensity towards anxiety is not successfully identified prior to flight, short- or long-acting BZDs may play an important role in achieving anxiolysis. Additional research is necessary before any of these techniques can be effectively applied in the commercial spaceflight realm, but the findings of this review suggest that successful mitigation may be achievable, and further provide direction for future study.

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Vita

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