Acceptability of Virtual Reality Experience by Health Care Providers for Improving Focus and Reducing Anxiety: A Pilot Trial.

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Aims, purpose, or objectives:

We propose to conduct a pilot study on the safety and impact of two nature-based virtual reality (VR) interventions on levels of anxiety and inattention.

Paradigms like this have been used previously to study the impact of VR on anxiety[1,2] but this specific intervention has not. Thus, it is reasonable to assume that it is feasible, but unique to the study of workplace anxiety and inattention, and in its design too.

The proposed investigation will apply two novel paradigms using proprietary VR (R-VR) interventions designed to reduce anxiety and inattention. We will explore whether this intervention is safe, and whether it can impact the stress, anxiety, and difficulty in focus of employees in the workplace. Results from this pilot study will be used to decide if a larger efficacy study with longer duration of daily VR experience will be developed.

The primary aims:

1) Evaluate the safety and acceptability of the R-VR

2) Evaluate the adherence to the R-VR

3) Evaluate the impact of using R-VR on anxiety and inattention levels

4) Compare the impact of two R-VR paradigms on anxiety and to correlate this impact with baseline self-efficacy

The major constructs that will be examined in this proposal are (1) Safety; (2) Anxiety; (3) Inattention; (4) Self-Efficacy. It is expected that this exploratory work will lay the foundation for future studies on anxiety and inattention interventions at work.

Background:

Is anxiety in the workplace relevant? According to large population-based surveys, up to 33.7 percent of the population is affected by an anxiety disorder during their lifetime[3]. In the workplace, millennials and people who fall into the "Gen Z" category are especially vulnerable[4], and 54 percent of workers under 23 said they felt anxious or nervous due to stress in the preceding month[5].

While some anxiety may improve job performance[6] by motivating people, many studies now document the detrimental impact of anxiety on job performance. Impostor syndrome[7], burnout[8], and decreased satisfaction with work[9] are just some of the negative impacts of anxiety. Also, much research also demonstrates that the greater the anxiety, the lower degree of hope and sense of possibility[10,11], with a subsequent sense of demoralization. In fact, anxious CEOs may be risk-averse verging on paranoid[12].

Furthermore, anxiety disorders are also very costly. The total costs of anxiety disorders were approximately $40 Billion in the US in the 1990s[13] and € 74.4 billion for 30 European EU countries in 2010[14]. The current costs are likely to be much higher.

Do we really need an intervention for anxiety at work? Although there are many conventional treatments for anxiety disorders, 40 percent of people who are treated relapse or are refractory[15]. Also, the percentage of people

with anxiety disorders who seek help is lower than 50 percent. Having an ancillary and readily available intervention for state anxiety in the workplace is likely to be helpful.

Why will we not focus on diagnoses per se? The category of "anxiety disorders" has raised much controversy recently, and there is a trend to examine traits in research that correlate with biology rather than consider diagnostic categories[16]. This is a feasibility study in a general population not focused on anxiety disorders but focused on the acceptability of such an intervention.

Why will we use nature-based interventions?
Studies indicate that forest walks are especially helpful in improving anxiety[17-19]. Even short-term exposures to nature decrease anxiety and improve happiness and wellbeing[20-24].

In a recent systematic review[25], many studies indicate that VR was an effective form of therapy for mental disorders compared to "treatment as usual". In addition, there are an increasing number of studies that have demonstrated that VR may be helpful for anxiety[26,27]. Specifically, it has been shown to be useful where worry is excessive[28], for social anxiety, post-traumatic stress disorder, and panic attacks[26].

For these reasons, combining nature-based interventions with VR is a potentially feasible approach to decrease anxiety in the workplace.

While the exact mechanism is unknown, some preliminary data indicates that this might occur by shifting proportional power from higher Beta frequencies into lower Beta frequencies, and significantly reduced broadband Beta activity in the anterior cingulate cortex[2]. And even after one session of VR, there is decreased activity in the dorsolateral prefrontal cortex and medial prefrontal cortex that increases over subsequent sessions[29].

Study Design and Methods

Design: This is a single blinded randomized cross-over study. The participants will be randomly assigned the order of the paradigms viewed in the R-VR or as videos on the computer. The randomization will be through REDCap, as programmed by the study statisticians. The R-VR with the pre-programmed paradigms and corresponding non-VR videos will be labelled A through D. The coordinators will be informed via REDCap about which the experience to provide the participants for each of the study visits: A-D for Visits 1-4.

Data Collection

- Participants will complete study surveys/questionnaires through REDCap. The coordinator will provide the iPad digital or paper copy version of the survey/questionnaire to the participant for the in-person visits and by email link or phone interview for the remote visits.

- Survey data collection in this study will utilize REDCap[30]. The only anticipated paper source documents will be if participant chooses to complete surveys via paper copy or phone collection, which will then have select variables entered directly into the REDCap data entry system. All other data collection will be entered directly into this password protected system.

Visit Flow and Timeline

	Day 0	Day 1			Day 4			Day 7			Day 10		
Visit Number	V0[2]	V1a[2]		V1b	V2a		V2b	V3a		V3b	V4a		V4b
		+ 0 day to +7 days from Consent	VR/Video	Immediately following VR/Video	Prior to VR/Video	VR/Video	Immediately following VR/Video	Prior to VR/Video	VR/Video	Immediately following VR/Video	Prior to VR/Video	VR/Video	Immediately following VR/Video
Informed Consent	X[1]												
Inclusion/Exclusion	X												
Demographics Form	X												
Medical History	X												
Adverse Events	X	X			X			X			X		
Concomitant Medications	X	X			X			X			X		
R-VR Intervention			X			X			X			X	
Brief Resilience		X			X			X			X		
Evaluate Response to the VR experience (HUMAN)		X		X	X		X	X		X	X		X
Emotional distress		X		X	X		X	X		X	X		X
Cognitive Function		X		X	X		X	X		X	X		X
Self-efficacy		X			X			X			X		
Anxiety		X		X	X		X	X		X	X		X
Satisfaction Survey													X

[1]Consent can be completed digitally in person or through remote consenting
[2]Visit 0 and Visit 1 can occur on same day or on separate occasions at the participant's convenience.

Assessments

Study Entry Screen/Safety:

- Demographics Form: This form will collect demographics (age, sex, education, marital status, job title), and other lifestyle history of the research participant.
- Medical History Form: This form will collect history of comorbid conditions such as head injury, seizures, major mental illness or anything that could interfere with the VR experience (e.g. eye sight). This information will be collected via self-report and health record abstraction.
- Adverse Events: Pre-post measures will be obtained for dizziness; stomach awareness; headaches; eyestrain and lightheadedness; nausea; seizures in individuals with photosensitivity; disorientation; temporary (short term) loss of spatial awareness.
- Concomitant Medications: Current medications (name, dosing, and indications) will be collected at every patient encounter.

Outcomes:

- Anxiety: *State-Trait Anxiety Inventory (STAI-Y1)*[31-35] This 20 item self-report measure indicates the intensity of feelings of anxiety; it distinguishes between state anxiety (a temporary condition experienced in specific situations) and trait anxiety (a general tendency to perceive situations as threatening). This uses a 4 point visual analog scale and the participant indicates how they feel in the moment (1=not at all to 4=very much so).
- Brief Resilience Scale (6 item)[36]: This brief 6 item survey is a validated way to assess resilience (ability to bounce back or recover from stress). It uses a 5 point visual analog scale to measure ability to bounce back where 1 is 'strongly disagree' and 5 is 'strongly agree' with a resilience focused statement.

- Human (7 items): This form has been developed by the Reulay sponsor and is used by the sponsor to individualize the Virtual Reality Experience to each person depending on the issues the person needs addressed. It provides 7 options and the participant will indicate the level of which each item is a current issue from 1= not at all to 5=a great deal. For this study, we will administer this questionnaire and evaluate the participant response to the two VR experiences based on how they responded to this survey.
- Emotional Distress: Adapted from the Emotional Distress-short form 7a (7 items)[37]. The *PROMIS Anxiety* item banks assess self-reported fear (fearfulness, panic), anxious misery (worry, dread), hyperarousal (tension, nervousness, restlessness), and somatic symptoms related to arousal (racing heart, dizziness). Anxiety is best differentiated by symptoms that reflect autonomic arousal and experience of threat. Only one behavioral avoidance item is included in the adult item bank; therefore, behavioral fear avoidance is not fully evaluated. The anxiety measures are universal rather than disease-specific. The original adult short form (7a), which is being used in this study was constructed by the domain team with a focus on representing the range of the trait and also representing the content of the item bank. Domain experts reviewed short forms to give input on the relevance of each item. Psychometric properties and clinical input were both used and likely varied in importance across domains. Each item on the measure is rated on a 5-point scale (1=never; 2=rarely; 3=sometimes; 4=often; and 5=always) with a range in score from 7 to 35 with higher scores indicating greater severity of anxiety. The original form instructed participants to think about the past seven days, but for purposes of this study, we will reword the question to focus on the current time ('now'). Therefore due to the change in directions of the reference point, our version of this measure is unvalidated and cannot be compared to the general population.
- Cognitive Function short form 6a (6 items)[37] : The *PROMIS Cognitive Function and Cognitive Function Abilities Subset* item banks assess patient-perceived cognitive deficits. Facets include mental acuity, concentration, verbal and nonverbal memory, verbal fluency, and perceived changes in these cognitive functions. The extent to which cognitive impairments interfere with daily functioning, whether other people observe cognitive impairments, and the impact of cognitive dysfunction on quality of life are also assessed.
- Self-efficacy (Short Form 4a – 4 items)[37]: This *PROMIS Self-efficacy Scale* defines self-efficacy as confidence in one's ability to successfully perform specific tasks or behaviors. It assesses confidence in one's ability to successfully perform specific tasks or behaviors related to one's health in a variety of situations. Each item on the measure is rated on a 5-point scale (1=I am not at all confident; 2=I am a little confident; 3=I am somewhat confident; 4=I am quite confident; 5=I am very confident)
- Satisfaction with the program: This questionnaire is adapted from *Was it Worth it Questionnaire (WIWI)*[38] and the *Reulay Qualitative Survey (RQS)* to measure study and RV satisfaction. It will be administered to the participants prior to discharge after completing the intervention at the end of the study, probing their satisfaction with the research study. These data could be used to assess the feasibility of the intervention by asking the patient if the entire research experience was worth it for them.

Acceptability and Adherence to Intervention:

- Acceptability will be measured through the patient satisfaction survey at the end of the study.
- Adherence to the R-VR will be assessed by collecting attendance for study visits 1-4.

Resources

REDCap will be utilized for data collection using created online forms. Clinician investigators will provide medical oversight. Tools needed for this intervention include one R-VR for each paradigm for a total of 2 R-VRs and a computer for the non VR experiences.

Study Design
We will use standardized procedures to ensure uniform instructions and support for all participants for the recruitment, screening, and study entry.

Recruitment
Participants will be recruited from Mayo Clinic healthcare professionals. We propose to recruit, consent and screen a convenient sample of 36 participants through IRB approved contact materials in order to enroll 24 to study. All participants who respond to the recruitment message will be pre-screened for inclusion and exclusion criteria via a telephone pre-screen. Those who meet criteria will be invited to a consent visit followed by a study screening visit. After consent and screening has taken place, participants who meet all study entry criteria will be invited to participate in the study.

Consent and Screen
Study coordinator will discuss possible participation with the potential participant who has expressed an interest in the study. The study coordinator will begin by introducing the study details, and after determining that the participant has continued interest in study participation, will move on to the study consent. If the participant chooses to consent, the study coordinator will screen the participant for study entry inclusion/exclusion criteria. If study entry criteria are met, the participant will begin their study participation. They will be asked to complete the study surveys/questionnaires, and after this is completed the participant will be instructed on the R-VR device and the video viewing experiences.

Video Experience Procedure

Participants will be scheduled for a 30-min office visit. After a verbal description of the study process and completion of IRB consent form, participants will complete the demographic and other baseline questionnaires.

The coordinator will instruct the participant on certain procedures dependent on the study participant's randomization and visit:

R-VR Experience: Study participant will be asked to complete a set of questionnaires, following completion they will be seated in a swivel chair in the center of the research room, given basic instruction on the VR headgear *[Oculus Quest],* and then offered the opportunity to experience the intervention event. The approximately 10 minute VR event involves one of two scenes (randomly selected by REDCap): Scene 1 is designed for relaxation in nature with natural scenery such as trees, streams and deer, or Scene 2 designed to help the participant focus with natural scenery such as glowing embers and fireflies. After a VR experience, the headgear will be removed and the participants will be asked to complete a second round of questionnaires.

Computer Video Experience: Study participant will be asked to complete a set of questionnaires, following by being seated at a computer and asked to watch a video with one of two scenes: (Scene 1) natural scenery such as trees, streams and deer; (Scene 2) natural scenery such as glowing embers and fireflies. After this viewing they will be asked to complete a set of surveys.

All will be remunerated up to $40 at the end of their study participation. This amount will be prorated based on the number of visits completed

This process will provide a within-participant control, allowing us to investigate whether the VR experience is safe and results in significantly more change than the Video experience.

Target accrual: 24 to be randomized (36 to be consented and screened).

Participant population: 24 adults

Inclusion Criteria:

1. 18 years of age or older at the time of consent
2. Healthcare Professional at Mayo Clinic
3. Not pregnant by participant self-report at time of consent
4. Have the ability to provide informed consent
5. Have no contraindicated comorbid health conditions as determined by the clinical investigators

Exclusion Criteria:

1. Currently (within the past 3 weeks) been practicing mindfulness training on a weekly/regular basis
2. Currently (within the past 3 weeks) been undergoing an additional program (e.g. CAM) to improve quality of life
3. Currently (within 3 weeks) been enrolled in another clinical or research program (e.g. CAM) which impacts the patients' QOL, stress or anxiety
4. Currently has photosensitivity
5. Cannot tolerate virtual reality experiences
6. An unstable medical or mental health condition as determined by the physician investigator (e.g. pre-existing eye strain, seizures, dizziness, nausea)

Data Analysis

Power Statement: The sample size for this pilot investigation (N=24) was established after considering both the statistical implications and the amount of project effort and resources required to recruit and study this unique participant population.

Data Analysis Plan: Data related to participant recruitment will be summarized, including the frequency of calls and the reasons for failing screening criteria. In all cases, data will be summarized using mean ± SD for continuous variables and frequency percentages for nominal variables. Details will be documented and summarized for any participants who experience adverse events or are unable to complete the 10-minute VR experience for any reason. The percentage of participants who undergo the initial VR experience (V2) but discontinue study participation without returning for the 2nd VR experience (V3) will be summarized and compared between scenes using Fisher's exact test. Anxiety, stress, cognition will be assessed immediately before/after and 24 hours following each VR experience. Within and between group comparisons will be performed using appropriate repeated measures analyses (e.g. paired t-test, repeated measures ANOVA) taking into account the two group repeated measures cross-over study design. In all cases, findings will be summarized using point estimates and corresponding 95% confidence intervals.

References

1. van Bennekom MJ, Kasanmoentalib MS, de Koning PP, Denys D. A Virtual Reality Game to Assess Obsessive-Compulsive Disorder. *Cyberpsychol Behav Soc Netw.* 2017;20(11):718-722.
2. Tarrant J, Viczko J, Cope H. Virtual Reality for Anxiety Reduction Demonstrated by Quantitative EEG: A Pilot Study. *Front Psychol.* 2018;9:1280.

3. Bandelow B, Michaelis S. Epidemiology of anxiety disorders in the 21st century. *Dialogues Clin Neurosci.* 2015;17(3):327-335.
4. Brown RL, Richman JA, Rospenda KM. Economic Stressors and Psychological Distress: Exploring Age Cohort Variation in the Wake of the Great Recession. *Stress Health.* 2017;33(3):267-277.
5. Shellenbarger S. The Most Anxious Generation Goes to Work. Wall Street Journal. https://www.wsj.com/articles/the-most-anxious-generation-goes-to-work-11557418951. Updated 09 May 2019. Accessed 31/07/2020.
6. Cheng BH, McCarthy JM. Understanding the dark and bright sides of anxiety: A theory of workplace anxiety. *J Appl Psychol.* 2018;103(5):537-560.
7. Bravata DM, Watts SA, Keefer AL, et al. Prevalence, Predictors, and Treatment of Impostor Syndrome: a Systematic Review. *J Gen Intern Med.* 2020;35(4):1252-1275.
8. Virga D, Schaufeli WB, Taris TW, van Beek I, Sulea C. Attachment Styles and Employee Performance: The Mediating Role of Burnout. *J Psychol.* 2019;153(4):383-401.
9. Yilmaz A. Burnout, job satisfaction, and anxiety-depression among family physicians: A cross-sectional study. *Journal of Family Medicine and Primary Care.* 2018;7(5):952-956.
10. Baryshnikov I, Rosenstrom T, Jylha P, et al. State and trait hopelessness in a prospective five-year study of patients with depressive disorders. *J Affect Disord.* 2018;239:107-114.
11. Gozuyesil E, Karacay Yikar S, Nazik E. An analysis of the anxiety and hopelessness levels of women during IVF-ET treatment. *Perspect Psychiatr Care.* 2020;56(2):338-346.
12. Manor M, Wowak A, V.O. B, Gomez-Mejia LR. How Anxiety Affects CEO Decision Making. Harvard Business Review. Decision Making Web site. https://hbr.org/2016/07/how-anxiety-affects-ceo-decision-making. Updated 19 July 2016. Accessed 31 July 2020.
13. Greenberg PE, Sisitsky T, Kessler RC, et al. The economic burden of anxiety disorders in the 1990s. *J Clin Psychiatry.* 1999;60(7):427-435.
14. Gustavsson A, Svensson M, Jacobi F, et al. Cost of disorders of the brain in Europe 2010. *Eur Neuropsychopharmacol.* 2011;21(10):718-779.
15. Roy-Byrne P. Treatment-refractory anxiety; definition, risk factors, and treatment challenges. *Dialogues Clin Neurosci.* 2015;17(2):191-206.
16. Lilienfeld SO, Treadway MT. Clashing Diagnostic Approaches: DSM-ICD Versus RDoC. *Annu Rev Clin Psychol.* 2016;12:435-463.
17. Koselka EPD, Weidner LC, Minasov A, et al. Walking Green: Developing an Evidence Base for Nature Prescriptions. *Int J Environ Res Public Health.* 2019;16(22).
18. Hansen MM, Jones R, Tocchini K. Shinrin-Yoku (Forest Bathing) and Nature Therapy: A State-of-the-Art Review. *Int J Environ Res Public Health.* 2017;14(8).
19. Song C, Ikei H, Miyazaki Y. Physiological Effects of Visual Stimulation with Forest Imagery. *Int J Environ Res Public Health.* 2018;15(2):213.
20. Bratman GN, Hamilton JP, Hahn KS, Daily GC, Gross JJ. Nature experience reduces rumination and subgenual prefrontal cortex activation. *Proc Natl Acad Sci U S A.* 2015;112(28):8567-8572.
21. Keniger LE, Gaston KJ, Irvine KN, Fuller RA. What are the benefits of interacting with nature? *Int J Environ Res Public Health.* 2013;10(3):913-935.
22. Capaldi CA, Dopko RL, Zelenski JM. The relationship between nature connectedness and happiness: a meta-analysis. *Front Psychol.* 2014;5:976.
23. Hartig T, Mitchell R, de Vries S, Frumkin H. Nature and health. *Annu Rev Public Health.* 2014;35:207-228.
24. Gascon M, Triguero-Mas M, Martinez D, et al. Mental health benefits of long-term exposure to residential green and blue spaces: a systematic review. *Int J Environ Res Public Health.* 2015;12(4):4354-4379.

25. Valmaggia LR, Latif L, Kempton MJ, Rus-Calafell M. Virtual reality in the psychological treatment for mental health problems: An systematic review of recent evidence. *Psychiatry Res.* 2016;236:189-195.
26. Maples-Keller JL, Bunnell BE, Kim SJ, Rothbaum BO. The Use of Virtual Reality Technology in the Treatment of Anxiety and Other Psychiatric Disorders. *Harv Rev Psychiatry.* 2017;25(3):103-113.
27. Oing T, Prescott J. Implementations of Virtual Reality for Anxiety-Related Disorders: Systematic Review. *JMIR Serious Games.* 2018;6(4):e10965.
28. Gorini A, Pallavicini F, Algeri D, Repetto C, Gaggioli A, Riva G. Virtual reality in the treatment of generalized anxiety disorders. *Stud Health Technol Inform.* 2010;154:39-43.
29. Landowska A, Roberts D, Eachus P, Barrett A. Within- and Between-Session Prefrontal Cortex Response to Virtual Reality Exposure Therapy for Acrophobia. *Front Hum Neurosci.* 2018;12:362.
30. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of biomedical informatics.* 2009;42(2):377-381.
31. Gaudry E, Vagg P, Spielberger CD. Validation of the State-Trait Distinction in Anxiety Research. *Multivariate Behav Res.* 1975;10(3):331-341.
32. Greene J, Cohen D, Siskowski C, Toyinbo P. The Relationship Between Family Caregiving and the Mental Health of Emerging Young Adult Caregivers. *J Behav Health Serv Res.* 2017;44(4):551-563.
33. Ugalde A, Krishnasamy M, Schofield P. The relationship between self-efficacy and anxiety and general distress in caregivers of people with advanced cancer. *J Palliat Med.* 2014;17(8):939-941.
34. State-Trait Anxiety Inventory. In: *The Corsini Encyclopedia of Psychology.*1-1.
35. Arnau RC, Broman-Fulks JJ, Green BA, Berman ME. The Anxiety Sensitivity Index--Revised: confirmatory factor analyses, structural invariance in Caucasian and African American samples, and score reliability and validity. *Assessment.* 2009;16(2):165-180.
36. Smith BW, Dalen J, Wiggins K, Tooley E, Christopher P, Bernard J. The brief resilience scale: assessing the ability to bounce back. *Int J Behav Med.* 2008;15(3):194-200.
37. Northwestern University. Health Measures: Transforming How Health is Measured. https://www.healthmeasures.net/. Published 2020. Accessed June 15, 2020.
38. Chauhan C, Atherton PJ. Patient satisfaction with participation in phase II/III NCCTG clinical trials: Was it worth it? (N0392). . *J Clin Oncology.* 2012a;30(15_Supplement):6133.