Virtual Reality Behavioral Activation: An Intervention for Major Depressive Disorder

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Protocol Director:
Margot Paul, M.S.

Academic Sponsor:
Kim Bullock, M.D.

Other Personnel:
Jeremy Bailenson, Ph.D.
[redacted]

Research Site:
Stanford School of Medicine, Department of Psychiatry & Behavioral Sciences
401 Quarry Rd, Palo Alto, CA 94304

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1. Purpose of the Study and Background

1.1 Purpose of the Study

The primary aims of this study are to assess the feasibility, acceptability, and tolerability of a virtual reality (VR) behavioral activation (BA) treatment for individuals diagnosed with major depressive disorder (MDD). The secondary aim of this study is to explore the efficacy of using VR to deliver BA therapy to a clinical MDD population.

The primary hypothesis of this study is that VR is an acceptable, feasible, and safe way to deliver a BA intervention for individuals diagnosed with MDD. Acceptability will measure the participant's desire to continue using the VR treatment after the study ends, the participant's satisfaction with the VR treatment, the participant's use of the headset, and the participant's acceptance of VR treatment. Feasibility will look at how well VR can integrate into the BA therapy. Tolerability will measure simulator sickness and agitation while using the VR headset.

A secondary hypothesis is that VRBA will have stronger effects than BA treatment as usual or a waitlist control in treating individuals with MDD due to increased homework compliance. This is due to the research that has illustrated that homework compliance is one of the strongest predictors of treatment outcomes for BA. This hypothesis will be assessed by running t-tests comparing the change in PHQ-9 scores at timepoints across the three study arms.

This study will also comment on the following questions: Can one successfully deliver BA without the movement component, simulating just the experience of pleasure/ mastery? Does VRBA lead people to want to engage in real-life activities? Is the active ingredient of BA emotion or movement? Movement during the VRBA will be measured with the headset.

1.2 Study Significance

Little to no research has been done to elucidate the role of VR technology in lieu of real-world behavioral activation. This study will lay the groundwork for future studies to examine the role that VR may play in improving mood in clinical populations that are unable to perform real-world behavioral activation because of physical and/or psychological limitations.

1.3 Background

Major depressive disorder (MDD) is one of the most common mental disorders in the United States. The lifetime prevalence of MDD is estimated to be 12% (Kessler et al., 2011) and it is the 11th greatest cause of disability and mortality in the world (Murray et al., 2012). Current treatment includes both cognitive behavioral therapy (CBT) and pharmacological intervention. There is strong evidence for the efficacy of a very simple type of CBT for depression that requires no active cognitive abilities from participants and can be delivered by primary care providers. This type of therapy is called Behavioral Activation (BA) (Dimidjian et al., 2011). Research has shown BA to be more effective than cognitive therapy alone and equivalent to

medication for treating depression in participants (Dimidjian et al., 2006; Scogin et al., 2005; Spates, Pagoto, & Kalata, 2006). However, many participants are unable to complete BA therapy due to lack of access to trained providers, physical constraints, diminished motivation, or geographical or financial reasons. Increasing access to mental health care using technology such as a Virtual BA therapy may provide a solution to these barriers.

Behavioral Activation encourages participants to change their moods by changing behavior and increasing sensory stimulation and positive emotions. BA therapy begins with monitoring a participant's current activity and identifying positive activities that can be added into the participant's daily schedule. These pleasant activities can be as simple as soaking in a bathtub, going to the mall, lying on the beach, or going fishing. These activities are then scheduled into the participant's daily routine, and progress is tracked. The list of activities is modified as necessary and challenges and barriers are problem-solved for each participant.

Virtual Reality (VR) technology now allows one to create and experience realistic and immersive virtual environments in which people can move around freely and interact with their surroundings. Compared to other mediums, VR is a very effective tool for eliciting feelings of presence: the user's subjective feeling of being inside a virtual environment. In part because of its ability to elicit presence, VR has been leveraged to deliver mental health interventions, including exposure-based therapies for participants with anxiety. VR is ideal for exposure therapy because participants are realistically immersed in a feared environment that is tailored to match their specific phobias (Maples-Keller, Runnell, Kim, & Rothbaum, 2017). For similar reasons, VR may also be ideal for delivering BA therapy: individuals can be immersed in environments that evoke strong feelings of enjoyment, mastery, and pleasure. These environments can be tailored to match each individual's list of ideal, positive activities. VR may also be ideal for delivering BA because it makes an incredibly wide range of activities easily and immediately accessible and can include pleasurable activities that may be impossible to complete in the real world (e.g. scuba-diving the Great Barrier Reef).

Within a clinical MDD population, VR-BA may be especially ideal for individuals who lack the motivation to engage in real-world BA. In this setting, VR-BA may either replace or act as a steppingstone to real-world BA. Standardizing and operationalizing a BA treatment to be self-administered may also be a cost-effective way of preventing and treating MDD. This may be especially important in areas where access to care is a problem for MDD treatment.

1.4 References

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2. Criteria for Subject Selection

2.1 Number of Subjects: 30

2.2 Gender of Subjects: All genders will be included and accepted in the study.

2.3 Age of Subjects: Participants must be over the age of 18 years old.

2.4 Racial and Ethnic Origin: No enrollment restrictions based on race or ethnicity.

2.5 Inclusion Criteria:

1. Participant must meet DSM V criteria for MDD
2. 18 years of age or older
3. English speaking

2.6 Exclusion criteria

1. Substance Use Disorders in past year
2. Any psychosis or bipolar I disorder
3. Any seizure in the last 6 months or untreated epilepsy
4. Current suicidal urges and intent
5. Current nonsuicidal self-injury or parasuicidal behavior

3. Methods and Procedures

3.1 Procedure

Participants will be recruited from the clinic waitlist or through the study flyer. A total of 30 participants will be recruited, about 10 participants per study arm. These participants will be given the contact information of the protocol director. Upon reaching out to the protocol director, an informational phone script will be read to determine study eligibility and subject interest.

If subjects are interested and present with symptoms of depression, they will be invited to Stanford School of Medicine, Department of Psychiatry & Behavioral Sciences for an intake session. This session will include obtaining informed consent, the Mini International Neuropsychiatric Interview, and completing the demographic questionnaire. If subjects meet study eligibility, they will be randomized into either the VRBA, BA treatment as usual, or waitlist control arm of the study using 5 opaque, concealed envelopes in sets of 6 to preserve balance throughout the study. Participants will have a 1 in 3 chance of being randomized into each group. Participants will then be scheduled for their first treatment appointment.

The VR intervention will follow the protocol for Behavioral Activation (BA). Participants in the BA treatment as usual or VRBA arms of the study will meet with their clinician once per week for 50 minutes to receive BA therapy. These participants will complete the PHQ-9 at the

beginning of each session. If item 9 is endorsed, a risk assessment will be completed in real-time and appropriate actions will be taken.

In the first session, psychoeducation around the connection between behavior and mood will be discussed. Participants will then be introduced to BA. Participants will consider activities they enjoy as well as be provided with an activity list. Participants will be asked to select at least four activities that are highly enjoyable to schedule into their upcoming week. The VRBA participants will be required to choose VR activities for the week and the BA treatment as usual participants will be required to choose real-life activities to participate in. The VR participants will complete an activity in VR during session, in order to learn how to use the headset, which they will take home. Each time the participant finishes an activity in VR, he/she will be asked to complete a questionnaire assessing "spatial presence," "simulator sickness," "agitation measure," and acceptability. Participants will also be asked to rate their mood on a scale of 1-10 (1=worst they ever felt; 10=best they ever felt) before and after their chosen activity. During session 2 and 3, clinicians will check in regarding goal attainment, work on barriers to completion of activities, assess depression scores, and introduce a new activity goal. During session 4, the treatment and skills will be reviewed, and feedback will be attained.

The participants randomized to the waitlist control group will be administered the PHQ-9 via phone on a weekly basis for four weeks. If item 9 is endorsed, a risk assessment will be conducted in real-time, and proper measures will be taken in accordance with risk. After the four weeks are completed, these participants will be given the option to simply remain on the clinic waitlist or choose to partake in 4 weeks of VRBA or BA treatment as usual. Only the data during their time as a waitlist control will be used in the study.

4. Data Safety Monitoring Plan

As this is a case series within standard of care procedures, steps to minimize risks to the confidentiality of identifiable information will be taken as with all HIPPA compliant services delivered at the Clinic. Data will all be labeled with the participants' assigned ID number. Protected Health Information will be kept separate from data and ID numbers in a Stanford University School of Medicine encrypted database to which only the PI and research assistants will have access. Psychological effects of study participation or breeches in confidentiality will be monitored and discussed at research meetings. There is a slight risk of motion sickness so participants will be closely monitored while immersed in the virtual scene, and if there is any discomfort they will be removed from the virtual environment. Participants are free to discontinue participation at any time. Any situation requiring medical attention will be promptly provided.

Given that participants enrolled are clinically depressed, suicidal ideation will be assessed each session. If it is revealed that a participant is expressing suicidal ideation, the clinician will conduct a thorough risk assessment in real time and a safety plan will be created. If it is determined the participant is an imminent danger to themselves, the clinician will initiate a 5150 hold and walk the participant to the hospital.

5. Preliminary unpublished data: There is no preliminary data to date.