Virtual Reality Behavioral Activation: An Intervention for Major Depressive Disorder NCT04268316 April 13, 2021

Aim 1: To evaluate whether using VR to administer a brief BA protocol is a feasible, acceptable, and tolerable treatment for individuals diagnosed with MDD.

Aim 1 Analysis: The feasibility, or degree to which VR could successfully be integrated into the brief BA protocol, was measured by commenting on qualitative barriers to use observed. Barriers were assessed by rates of dropout, adverse events, the number of times the headset was used, and the level of presence experienced in the headset, all of which were represented in a table, as recommended by Birckhead et al. (2019). Level of presence was obtained by participant report from a Likert scale of 0 (not at all) through 4 (very strongly) for each question; and with three questions, there was a possibility of yielding a score between 0 and 12. The average total presence for each participant, intend-to-treat (ITT) participants, and protocol completers were then calculated and placed into a table. The average presence experienced was also calculated as a percentage by dividing the average score by 12 (the maximum score). Acceptability of the VR BA treatment was measured by participant report using the TAM, with the agreeance choice on the Likert scale represented from 0 (strongly disagree) through 4 (strongly agree). The number of questions in each category determined the outcome range (either 0-12 for three questions or 0-16 for four questions). Each participant's scores were then averaged and placed into a table, along with the average ITT participants and protocol completers' scores. The average percentage of acceptance was also calculated by dividing the average score by the maximum score in the outcome range. In order to determine the degree of

acceptance, as labeled on the scale, the average score was then scaled back depending on the number of questions. For example, the "Perceived Usefulness" category included three questions, yielding a potential range of 0 to 12, so an average score of 10 would be divided by 3 to assess the degree of acceptance (in this case it would yield a score of 3.33, which would correlate to "agree" on the Likert scale). Physical tolerability of the VR headset was assessed by participant report using the SSQ, and the emotional tolerability of the VR headset was assessed by participant report using the BAM, again represented in tables. Physical tolerability was broken into each item and ranged from 0 (no more than usual) through 3 (severely more than usual) for each item. Each participant's scores were averaged and placed into a table, along with the average ITT participants and protocol completers' scores. The total percentage tolerability rating for a given activity was calculated by dividing a participant's score by 48, since there were 16 items, yielding a potential range of 0 to 48. For example, if a participant endorsed *nausea* slightly more than usual (1), *sweating* moderately more than usual (2), and *headache* slightly more than usual (1) during the VR activity labeled "Puppies," then his/her percentage score would be calculated by diving 4 by 48, to yield 8.33% intolerability or 91.67% tolerability during that activity. The percentage of intolerability for each symptom category was similarly calculated by dividing the average score by the maximum potential score of 3. The average scores for physical tolerability were summed for each participant and placed into a table, along with the average emotional tolerability scores of each participant. Emotional tolerability was scored from 1 (strongly disagree) to 7 (strongly agree) per question; and with three questions, there was a possibility of yielding a score between 3 and 21. These scores were rescaled to a range of 0 to 18 by subtracting 3 from all scores. The percentage of physical intolerability and

emotional intolerability were calculated by dividing the average scores by the highest potential score (48 for physical tolerability and 18 for emotional tolerability).

Aim 2: To assess whether VR BA is efficacious in treating the symptoms of MDD compared to BA as usual or a waitlist control.

Aim 2 Analysis: In order to determine any initial clinical efficacy of the VR BA treatment compared to BA treatment as usual and a waitlist control, participants' depression scores were measured using the PHQ-9 at four time points. With the goal of randomizing 30 participants, the average change between PHQ-9 scores at time 4 and time 1 for each of the three groups were going to be compared to one another. Example: Average change in PHQ-9 scores of group A (VRBA) was going to be compared to the average change in PHQ-9 scores of group B (BA treatment as usual). The average change in PHQ-9 scores of group A was going to be compared to the average change in PHQ-9 scores of group A was going to be compared to the average change in PHQ-9 scores of group A was going to be compared to the average change in PHQ-9 scores of group A was going to be compared to the average change in PHQ-9 scores of group A was going to be compared to the average change in PHQ-9 scores of group A was going to be compared to the average change in PHQ-9 scores of group A was going to be compared to the average change in PHQ-9 scores of group C (waitlist control). The average change in PHQ-9 scores of group C. This change was going to be determined using independent samples t-tests.

However, given the lower-than-expected sample size, in order to assess initial clinical efficacy of the VR BA treatment compared to the BA treatment as usual and control groups, each group's mean as well as each participant's PHQ-9 scores were graphically represented across time. Additionally, each group's mean PHQ-9 change scores from time one through time four were graphically represented.

Exploratory Aim 1: To evaluate whether engaging in an activity in VR increases mood more than engaging in an activity in real life.

Exploratory Aim 1 Analysis: In order to evaluate whether engaging in an activity in VR increased mood more than engaging in an activity in real life, the differences in mood before

and after each VR activity were cumulatively added across each participant and then divided by the number of activities completed, in order to find the mean. The same was done for the BA treatment as usual group. For example, a participant who completed three total activities and reported a pre-activity score of 5 and a post-activity score of 6 for activity one, a pre-activity score of 3 and a post-activity score of 5 for activity two, and a pre-activity score of 8 and a postactivity score of 7 for activity three, would have a difference of 1, 2, and -1 respectively. These numbers would be summed to a total difference of 2, and then divided by the number of activities (3), to yield an average score change of .67 pre- to post-activity. These averages were represented in a table. Additionally, the reported pre- to post-activity mood changes of participants in the VR BA and BA treatment as usual group were tallied and graphically represented.