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Suso-Ribera, Carlos[1]; Fernández-Álvarez, Javier[2]; García-Palacios, Azucena[1,3]; Hoffman, Hunter G.[4]; Baños, Rosa M.[3,5]; Quero, Soledad[1,3]; Botella, Cristina[1,3]

[1] Department of Basic and Clinical Psychology and Psychobiology. Jaume I University. Castellon (Spain)

[2] Università Cattolica del Sacro Cuore. Milan (Italy)

[3] CIBER of Physiopathology of Obesity and Nutrition CIBERobn, CB06/03 Instituto de Salud Carlos III, Spain

4 Virtual Reality Research Center at the Human Photonics Lab, Mechanical Engineering. University of Washington. Seattle (United States)

5 Department of Personality, Assessment, and Psychological Treatments. Valencia University. Valencia (Spain)

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Introduction: The present study aggregated data from three randomized control trials to explore the differential efficacy of three forms of exposure therapy, namely, in vivo (iVRET), virtual reality (VRET), and augmented reality (ARET), in the treatment of small animal phobia. Additionally, baseline patient characteristics were used to detect subgroups of patients who showed a differential response to certain treatment modalities. Methods: Primary measures were distance covered, anxiety during the behavioral avoidance test, and overall fear of small animals. A repeated-measures ANOVA was used to explore the overall treatment effect across the exposure modalities. A cluster analysis and an analysis of moderation were conducted to explore differential response to treatments. Results: The main study finding was that the three conditions were similarly efficacious in the treatment of small animal phobia for all study outcomes. Only for distance covered, our results revealed a tendency for iVET to be more effective than VRET and ARET in participants with worse performance on the BAT before treatment. Discussion: The present study findings provide further evidence for the comparable efficacy of the three forms of exposure. Our results also suggest that, overall, treatments are likely to be similarly effective, regardless of the individual baseline characteristics (i.e., fear, anxiety, and age), whereas pretreatment scores on distance covered in the avoidance test might be used to personalize treatments (iVET may be preferable when participants perform worse at pretreatment).

Key words: Virtual reality exposure therapy; augmented reality exposure therapy; in vivo exposure therapy; small animal phobia.

Introduction

Animal phobia (i.e., insects, snakes, birds, or other animals) is one of the most prevalent forms of specific phobias, especially in women. Lifetime rates of this disease range from 5% to more than 12%, depending on the study, with the highest prevalence rates in young adults.[1–4]

In vivo exposure therapy (iVET) is the treatment of choice for specific phobias, including animal phobia, as it has been shown to outperform all other forms of non-exposure psychosocial treatment. However, other forms of exposure treatment, such as virtual reality exposure therapy (VRET), have been found to be just as efficacious as iVET,[5] especially over time after treatment.[6]

Virtual reality and augmented reality are two technologies that can be used as alternatives to iVET. In the former, the patient is asked to interact with a computer-generated, three-dimensional environment or object. In the latter, a computer-generated virtual object is superimposed on reality.[7] The use of these alternative forms of exposure has been found to have some advantages over traditional iVET. For instance, some clinicians and patients are reluctant to use iVET because they find it cruel.[8,9] In fact, there is evidence suggesting that virtual reality has a much lower refusal rate than in vivo treatment.[10] In addition, VRET and augmented reality exposure therapy (ARET) offer ecological treatments when the availability of the feared stimuli is limited.[11]

There is currently extensive evidence for the effectiveness of VRET and ARET in the treatment of a wide range of mental disorders.[12,13] For instance, their use is now supported in post-traumatic stress disorder[14,15] and anxiety disorders,[16–18] including panic disorder, social anxiety disorder, and specific phobias.

Although some previous evidence suggests that alternative forms of exposure and traditional iVET are equally effective,[5] especially at follow-up,[6] this latter meta-analysis did not report separate effect sizes for the different forms of alternative exposure treatments (i.e., imaginal exposure, CAVE, and VRET), and neither of the two meta-analyses included data on augmented reality. Moreover, it is still unclear whether certain treatments might be more beneficial for a certain subset of patients (i.e., moderation). The goal of the present study is to compare the efficacy of three treatment modalities, namely, traditional iVET, VRET, and ARET, for small animal phobia, and investigate differential treatment efficacy as a function of baseline patient characteristics.

Methods

Research design and procedure

In this study, three datasets from previously published randomized controlled trials were compared (BLINDED). A summary of the studies included is shown in Table 1. All the studies included a VRET, an ARET, or an iVET group.

Measures

Behavioral Avoidance Test (BAT).[22] The BAT is an objective, observational test to measure clinical progress in overcoming phobias through exposure to the feared object. In all the studies, a sealed container containing a live cockroach or a spider was placed on a table inside a room. Participants were asked to enter the room and approach the spider as much as they could. Then, the distance covered was measured, and participants were asked to rate their anxiety level during the test. In BLINDED, the distance from the door to the container was 5 meters. In BLINDED and BLINDED, the

distance left to cover was measured in meters, whereas in the study by BLINDED, the distance left to cover was measured in feet. In BLINDED and BLINDED, a 101-point measure of anxiety was obtained, where 0 represented *no anxiety,* and 100 reflected *extreme anxiety*. The study by BLINDED used an 11-point scale ranging from 0 (*no anxiety*) to 10 (*extreme anxiety*).

The BAT was performed in a separate room from the treatment room. During the test, the experimenter waited outside the door to minimize the impact of his/her presence. Participants were informed that the BAT was used as an objective measure of their fear, and not as part of the therapy.

Fear of Spiders Questionnaire (FSQ).[23] Items on the FSQ are designed to assess patients' anxiety about spiders. In the study by BLINDED, the instructions were changed so that participants with fear of cockroaches referred to their feared small animal (i.e., cockroaches). Two of the studies used the full version of the FSQ, BLINDED, which consists of 18 items, whereas BLINDED used a reduced 6-item version. The same response scale, ranging from 1 (*does not apply to me*) to 7 (*very much applies to me*), was used in all cases. The FSQ has obtained excellent reliability and validity results in previous research.[24] The FSQ was administered both before and after exposure treatment.

Data analysis

First, all the variables were standardized to compare scores using different scales and numbers of items. The formula used was $z = (X - \mu)/\sigma$, where z is the standardized score with a mean of 0 and standard deviation of 1, X is the score that has to be converted, μ is the sample mean, and σ is the standard deviation.

Baseline imbalance was explored for all study outcomes (i.e., fear of the small animal, anxiety, and distance left to cover), in order to decide whether covariates would be needed in the repeated-measures analysis.[25] As Table 2 shows, baseline scores were comparable across conditions, and so there was no need to control for baseline ratings in the repeated-measures ANOVA. In the ANOVA, time and treatment condition were the within- and between-subject factors, respectively. Fear, anxiety, and distance were the dependent variables.

Finally, a series of two-step cluster analyses were performed to explore whether there were groups of cases in the data (i.e., groups who differed in their responses to treatment). In each analysis, the condition was included as a categorical variable. Three cluster analyses were performed, one for each outcome variable. For each outcome, pretreatment and posttreatment ratings of that outcome were included as continuous variables.

Results

The final sample consisted of 91 participants, including 32 from the ARET condition, 28 from the VRET condition, and 31 from the iVET condition.

As seen in Table 2, which presents the sociodemographic and clinical characteristics of the sample, most individuals were highly educated, young, and female.

Table 3 shows the participants' median scores for all study outcomes across conditions, along with the results of the baseline imbalance test. The Kolmogorov–Smirnov test and Levene's test revealed that assumptions of parametric data were violated (i.e., normality and homogeneity of variance). Hence, baseline imbalance across the three conditions

was explored by means of a Kruskal–Wallis test, which indicated that baseline scores were comparable across conditions for all outcomes ($H_{distance}$ (2) = 1.45, p = .485; $H_{anxiety}$ (2) = 0.78, p = .676; H_{fear} (2) = 1.84, p = .399), and so there was no need to use baseline scores of study outcomes as covariates in the repeated-measures ANOVA.

As Table 3 shows, the repeated-measures ANOVA revealed a significant effect of time for all study outcomes, namely, fear, F (1, 88) = 529. 26, p <.001, anxiety, F (1, 88) = 90.96, p <.001, and distance, F (1, 88) = 109.33, p <.001. There was a decrease in fear ($M_{pretreatment}$ = .82, $M_{posttreatment}$ = -.82), anxiety ($M_{pretreatment}$ = .52, $M_{posttreatment}$ = -.52), and distance left to cover ($M_{pretreatment}$ = .56, $M_{posttreatment}$ = -.56) over time. The largest change was revealed for fear (η_p^2 = .86), although all the effects of time should be interpreted as large (22).

Table 3 shows that the time*condition effect was not significant for any of the study outcomes, indicating comparable effects for VRET, ARET, and iVET.

Cluster analysis

The same three-factor solution was obtained for anxiety (condition = categorical variable; pretreatment and posttreatment anxiety = continuous variables) and fear (condition = categorical variable; pretreatment and posttreatment fear = continuous variables). Each cluster corresponded to one treatment condition (1 = ARET, n_1 = 32; 2 = VRET, n_2 = 28; and 3 = iVET, n_3 = 31). Median pretreatment anxiety scores were Mdn_1 = 0.54, Mdn_2 = 0.37, and Mdn_3 = 0.90. Median posttreatment anxiety ratings were Mdn_1 = -0.19, Mdn_2 = -.49, and Mdn_3 = -.92. Median pretreatment fear scores were Mdn_1 = 0.80, Mdn_2 = 1.02, and Mdn_3 = 0.72. Average posttreatment ratings for fear were Mdn_1 = -0.77, Mdn_2 = -0.77, and Mdn_3 = -0.79.

The cluster analysis for distance (condition = categorical variable; pretreatment and posttreatment distance = continuous variables) revealed a four-factor solution. Cluster 1 included all iVET participants (n_1 = 31). Clusters 2 and 4 included the majority of the ARET (n_2 = 29) or VRET participants (n_4 = 25). The third cluster included 6 participants (10% of the total sample), 3 from the ARET condition and 3 from the VRET group. Median pretreatment distance scores for clusters 1 to 4 were Mdn_1 = 0.63, Mdn_2 = 0.63, Mdn_3 = 1.89, and Mdn_4 = 0.63. Median scores at posttreatment were Mdn_1 = -.68, Mdn_2 = -.67, Mdn_3 = 1.07, and Mdn_4 = -0.77. A graphical representation of this four-factor solution is shown in Figure 1. The graphical display suggested that the common feature of individuals in cluster 3 might be poor posttreatment performance. Indeed, the Kruskall-Wallis test revealed a difference between clusters in distance covered at posttreatment, $H(3) = 31.59$, $p < .001$, but not at pretreatment, $H(3) = 3.63$, $p = .305$. A post-hoc Mann-Whitney test revealed a difference in posttreatment distance when comparing clusters 1 and 3 ($U < 0.01$, $Z = -5.61$, $p < .001$), 2 and 3 ($U < 0.01$, $Z = -5.80$, $p < .001$), and 3 and 4 ($U < 0.01$, $Z = -3.76$, $p < .001$). Effect sizes of these differences in posttreatment distance were calculated ($r = Z/\sqrt{n}$). All differences were found to be large (r_{13} = -.92, r_{13} = -.98, and r_{13} = -.68).

We compared differences in baseline measures between cluster 3 and the other 3 clusters together (n = 85) to better understand the poorer performance in posttreatment distance covered. We did not find group differences in age ($U < 223.50$, $Z = -0.51$, $p = .613$), duration of the fear ($U < 195.00$, $Z = -0.76$, $p = .764$), pretreatment anxiety ($U < 246.50$, $Z = -0.14$, $p = .891$), or pretreatment fear ($U < 183.00$, $Z = -1.15$, $p = .249$). We found a non-significant trend for pretreatment distance ($U < 143.50$, $Z = -1.80$, $p = .072$).

Median distances covered at pretreatment in cluster 3 (the one with poor performance on distance after treatment) and the other 3 clusters were 1.89 and 0.63, respectively. In our sample, a standardized distance of 1.89 should be interpreted as approximately 4 meters away from the feared animal (from an initial distance of 5 meters), whereas a standardized distance of 0.63 reflects a distance of 2 meters left to cover (from an initial distance of 5 meters).

Because there were no individuals from the iVET condition in cluster 3, and we found a trend toward a significantly higher baseline distance left to cover in this cluster, we explored whether iVET was more effective than VRET and ARET for individuals with high baseline scores on distance left to cover. A multivariate regression was performed with treatment condition (1=ARET or VRET; 2=in vivo) in the first block, baseline distance in the second block, and the interaction between condition and baseline distance in the third block. Posttreatment distance covered was used as the dependent variable. The model explained 10.2% of the variance in posttreatment distance covered, and the effect of the interaction term was marginally significant, $F(1) = 3.82$, $p = .054$, change in $R^2 = 2.9\%$, $B = -0.21$ (-0.420, 0.004), $p = .054$. A graphical representation of this marginally significant moderation effect is presented in Figure 2.

No moderation effect was found when the same analysis was performed for anxiety, $F(1) = 0.19$, $p = .667$, change in $R^2 < 0.1\%$, $B = -0.12$ (-0.682, 0.439), $p = .667$, and fear, $F(1) = 1.61$, $p = .208$, change in $R^2 < 0.1\%$, $B = -0.38$ (-0.981, 0.217), $p = .208$.

Discussion

This study aimed to study the differential efficacy of VRET, ARET, and iVET for the treatment of small animal phobia. Research had revealed that other exposure treatments, including VRET, were good alternatives to iVET for the treatment of specific

phobias,[5,6,16] including small animal phobia.BLINDED However, to the best of our knowledge, no study had compared the efficacy of the three treatment modalities together, and it was unclear whether subgroups of patients might show a differential response to certain treatments.

The results from the present study suggest that the three approaches may be equally efficacious in the treatment of behavioral (e.g., distance covered during the BAT) and psychological (i.e., anxiety during the BAT and fear) features of the disease. In our study, this similarity in the results was observed right after treatment, coinciding with the most recent meta-analysis on specific phobias.[5] A previous meta-analysis only indicated the comparability of traditional iVET and alternative forms of exposure at follow-up. [6] It is important to note, however, that alternative forms of exposure in this study included a mixture of different procedures (i.e., imaginal exposure, CAVE, and VRET), but no study on augmented reality, which might help to understand the differences found in our investigation and in the more recent meta-analysis.[5]

This study used cluster analysis and moderation analysis to explore whether subgroups of patients showed a differential response to the treatments. This is important because the detection of subgroups would provide evidence about how to maximize treatment effectiveness (i.e., personalized treatments) by selecting the treatment that has the most impact on each subset of individuals. Overall, our results suggest that the three treatment modalities are effective across different levels of patient characteristics, including age, fear, and anxiety during the BAT. The cluster analyses only revealed differences in the response to treatment for distance. Specifically, one group of individuals (n = 6) was found to differ from the other groups in distance covered after treatment. None of the poor-responding patients belonged to the iVET group, 3 received VRET treatment, and 3 participated in the ARET condition. Accordingly, a moderation

analysis revealed a marginally significant trend toward a superior efficacy of iVET when less distance was covered in the baseline BAT test. Although the implications of the results should not be overstated, it is possible that iVET is indicated more when individuals show worse performance on distance covered during the BAT test. Further research should explore the reliability of this finding, which might be important in personalizing treatments.

One of the strengths of the present investigation is that, after aggregating the three datasets used, the sample size was large compared to previous research. In fact, the most recent meta-analysis comparing VRET and iVET for the treatment of specific phobias revealed that the mean sample size for the 14 studies included was only 18.64 participants.[5] Our investigation intended to overcome this limitation of small sample sizes by aggregating data from three studies. However, this study is not free of limitations. First, there was very low variability in age and sex, and so generalization of the results to men and older samples should be done with caution. However, it is important to note that small animal phobia is more frequent in females and younger adults, so that these study findings may be relevant for a large percentage of patients. In addition, although cluster analyses are useful tools to identify groups of cases with a shared characteristic, it is also true that they are atheoretical, and their solution is not generalizable because it depends on the variables used. Hence, the results should be interpreted with caution, and replication is needed. Finally, although the aggregation of studies led to a considerable sample size, larger sample sizes are needed to explore whether certain treatments are more effective for a subset of patients, which is a key to personalizing psychological treatments. For example, our cluster and moderation analyses did not reveal different subgroups of patients as a function of baseline and

posttreatment anxiety and fear. However, larger sample sizes with greater variability, for example in sex, could test different moderators and grouping variables.

In spite of these shortcomings, our study findings may have important clinical implications because they support previous literature indicating that VRET and ARET are useful alternatives to traditional iVET treatments for small animal phobia. Considering that iVET treatments are more frequently refused by patients than VRET,[10] these findings are important because they provide clinicians with two equally efficacious alternatives to iVET.

It is important to note, however, that the implementation of VRET and ARET in clinical practice is still difficult. Research has revealed some resistance in implementing new digital technologies in clinical practice.[26] Moreover, virtual reality devices have traditionally been expensive, which might have restricted their use. Fortunately, this situation is already starting to change, and new trials are being carried out with inexpensive commercial devices.[27] It is important to make virtual reality devices accessible in terms of ease of use and price if their benefits are to be transferred from research to clinical practice. In this regard, it is likely that bigger sample sizes will be recruited for future studies, and, thus, it will be easier to establish differential responses to VRET and ARET.

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