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Focus Article

Efficacy of virtual reality exposure therapy for the treatment of dental phobia in adults: A randomized controlled trial

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ABSTRACT

Background: Although Virtual Reality Exposure Therapy (VRET) has proven to be effective in the treatment of various subtypes of specific phobia, there is limited evidence of its role in the treatment of dental phobia.
Method: A single-blind RCT was conducted among 30 randomized patients with dental phobia to either VRET or informational pamphlet (IP) condition. Primary outcome anxiety measures (VAS-A, MDAS and DFS) were evaluated at baseline, pre- and post-intervention, 1-week, 3-months and 6-months follow-up. Secondary outcome measures assessed were pre-post behavioral avoidance, temporal variations of heart rate and VR-experience during and post-VRET, and dental treatment acceptance in both conditions at 6-month follow-up.
Results: Intention to treat analysis, using a repeated measures MANOVA, revealed a multivariate interaction effect between time and condition ($p = 0.015$) for all primary outcome measures (all ps < 0.001). Only patients of the VRET condition showed a significant reduction in anxiety scores (mean reduction [s.d.]: VAS-A 44.4 [36.1]; MDAS 7.1 [5.4]; DFS 21.2 [13.1]) whereas the patients in the IP group did not (mean reduction [s.d.]: VAS-A −0.33 [7.7]; MDAS −0.33 [1.3]; DFS −1.9 [3.8]), $F(15, 14) = 3.3$, $p = 0.015$.
Conclusions: VRET was found to be efficacious in the treatment of dental phobia.

1. Introduction

Dental fear afflicts a significant proportion (5–15%) of the adult population, with approximately 4% satisfying the criteria for dental phobia (Hill, Chadwick, Freeman, O'Sullivan, & Murray, 2013; Humphris & King, 2011; Oosterink, de Jongh, & Hoogstraten, 2009). People with dental phobia typically avoid common dental treatment procedures and equipment such as extractions, dental drills and needles (Oosterink, de Jongh, & Aartman, 2008). Avoidance of dental treatment negatively impacts oral and general health by reducing dental attendance and uptake of dental care (Oosterink et al., 2008; Vermaire, de Jongh, & Aartman, 2008). Hence, timely and effective management of dental phobia is central to improving the oral health and quality of life of people experiencing dental phobia.

Virtual Reality Exposure Therapy (VRET) is an emerging technology that is increasingly being used for the treatment of patients suffering from specific phobia (Carl et al., 2018). During VRET patients are assisted to systematically confront their fear provoking objects and situations, within a well-controlled, computer generated virtual environment, until fear extinction occurs (Krijn, Emmelkamp, Olafsson, & Biemond, 2004). Extinction learning occurs through repeated confrontations to fear-eliciting stimuli in the absence of an aversive consequence, and can be measured by determining the initial or peak psychophysiological responses (Craske et al., 2008). For exposure therapy to be effective, it should be designed to violate core expectancies and administered until this is achieved (Craske, Treanor, Conway, Zbozinek, & Vervliet, 2014). Evidence suggests that higher initial fear responses and the enhancement of fear extinction through the modulation of behavioral parameters such as multiple contexts, mass extinction, or concurrent exciters are likely to lead to improved treatment outcomes and successful VRET (Botella, Fernandez-Alvarez, Guillen, Garcia-Palacios, & Banos, 2017). Also, for VRET to be effective and engaging for the patients, the virtual environment should consistently elicit the feeling of being present and real during the therapy (Botella et al., 2017). Recent research suggests that the application of VRET not only is less likely to cause deterioration in symptoms

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following therapy compared to wait-list controls (Fernandez-Alvarez et al., 2018), but also is associated with better patient acceptance compared to the gold standard, i.e., in vivo exposure therapy (Garcia-Palacios, Hoffman, See, Tsai, & Botella, 2001).

Preliminary evidence suggests that VRET may also be beneficial to individuals suffering from dental phobia (Botella et al., 2017; Gujjar, Sharma, & Jongh, 2017; Gujjar, van Wijk, Sharma, & de Jongh, 2018). We conducted a series of experiments to study the effects of VRET that showed VRET to be both effective in reducing dental trait anxiety and avoidance tendencies in patients with dental phobia (Gujjar et al., 2017, 2018). However, these VRET studies had several limitations, including the fact that the sample sizes were small (n = 1–5), outcome variables such as physiological arousal and habituation had not precisely been measured, and temporal variations of crucial factors that might have influenced the effectiveness of VRET (i.e., presence, realism, distress, and cybersickness experienced by patients during VRET) had not been evaluated.

The purpose of the present study was to address the limitations of earlier studies and to establish the efficacy of VRET in the treatment of dental phobia. The primary outcome measures were to evaluate and compare the state and dental trait anxiety scores post-intervention, and at 1 week, 3 month and 6 month follow-up, between VRET and the Informational Pamphlet (IP) condition. The secondary outcome measures evaluated the (a) difference between pre-post behavioral avoidance between VRET and the IP condition, (b) physiological Heart Rate (HR) changes during and post-VRET, (c) temporal variations in VR experience (presence, realism, cybersickness and distress) during and post-VRET, (d) dental treatment acceptance, and (e) the number of patients who no longer met the diagnostic criteria for dental phobia following the intervention in both conditions. Several hypotheses were tested to evaluate the effects of successful VRET. Firstly, we predicted that VRET would be associated with a significant reduction in patients' state anxiety and dental trait anxiety compared to the IP condition. Secondly, that VRET would be associated with a significantly greater reduction in behavioral avoidance compared to the IP, following intervention. Thirdly, that VRET would be associated with an increase in heart rate (HR) response (physiological arousal) during VRET, and a significant decrease in HR response (physiological habituation) after VRET. Fourthly, that patients would experience strong presence and realism with no cybersickness post-VRET. Finally, we hypothesized that a significantly greater proportion of the VRET participants would improve on their dental attendance and would no longer meet the diagnostic criteria of dental phobia, compared to their IP counterparts, 6 months following the intervention.

2. Methods

2.1. Design and participants

This study was a two-arm, parallel group RCT, conducted among patients visiting the outpatient services of the Faculty of Dentistry, SEGi University, Malaysia. The trial was approved by the ethical review board of SEGi University, Malaysia (Reference: EC01/14-01) and registered in the trial registry ISRCTN (Identifier: ISRCTN25824611). Fig. 1 shows the CONSORT flow chart for the study.

2.2. Screening

Adult patients visiting the university dental clinic a) who had not visited a dentist during the past 12 months or b) reported fear and avoidance towards dental procedures, were screened for the presence of dental phobia using the original MDAS (Humphris, Morrison, & Lindsay, 1995) questionnaire in English.

2.2.1. Inclusion criteria

Consenting patients with an MDAS score greater than or equal to 15 (n = 84) were assessed for dental phobia by KRG using the Phobia Checklist (Oosterink et al., 2009). Phobia Checklist is a screening instrument that has been validated against the structured clinical interview for DSM-IV with a sensitivity of 0.95, specificity of 0.99 and overall hit rate of 97% (Oosterink et al., 2009).

Eligible patients were asked whether they would be interested to participate in the study or wished to undergo their routine dental treatment at baseline (T0). Those patients who expressed interest were enlisted to participate in the trial. They required no emergency dental care nor there was any delay in their dental treatment.

2.2.2. Exclusion criteria

Patients with hearing or visual impairment such as stereoscopy blindness or nystagmus, known mental disorders such as psychosis, post-traumatic stress disorder (PTSD), developmental or intellectual disability, cognitive impairment, known balance disorders such as vertigo and cybersickness, previous history of epileptic seizures and a history of cardiac problems were excluded from participation. Also, patients who were undergoing, or had undergone, any form of cognitive behavioral therapy (CBT)-based intervention for their dental phobia, could not understand English or wore glasses of greater than plus 3.5 power were considered ineligible for the study.

2.2.3. Randomization

Patients who were deemed eligible for the study, having met the diagnostic criteria of dental phobia (n = 30), were randomized (allocation ratio of 1:1) to either the VRET or the IP condition using the SNOSE (Sequentially Numbered, Opaque Sealed Envelopes) method of allocation concealment (Doig & Simpson, 2005; Schulz & Grimes, 2002) at T0. Patients and the researcher (KRG) were aware of the allocated intervention. Blinding of statistician to the condition allocation was ensured by concealment of group identifiers on the main data file and using a separate data file for analyzing the physiological data of the VRET patients. Following randomization, patients were scheduled an appointment approximately within a week to undergo either VRET or to participate in the IP condition. KRG explained the purpose of the study to the patients by stating that the study compared the use of VRET and an informational pamphlet to determine whether this would have any effect on their dental anxiety. None of the patients in either of the conditions underwent the intervention and dental treatment concomitantly. However, after the intervention patients from both conditions were encouraged to schedule an appointment with a dentist either inside or outside the university clinic. Patients underwent several evaluations at different time points during the trial on a set of variables related to the research questions. These evaluations were done at baseline (T0), before intervention (T1) and directly after intervention (T2) along with follow up evaluations at 1 week (T3), 3 months (T4) and 6 months (T5) after the intervention.

2.2.4. Procedure

Eligible patients (n = 30, 60% women) signed a consent form to participate, after receiving detailed explanation about the study from KRG. Of all the patients, 16 were of Chinese descent, five were ethnic Malay, seven were of Indian descent and two originated from the Middle-east. At baseline evaluation (T0), approximately one week prior to the intervention, patients completed a questionnaire related to their demographic information, state anxiety and dental trait anxiety.

2.3. Intervention

On the scheduled day, prior to the intervention (T1), patients completed self-report questionnaires on state anxiety and dental trait anxiety in the waiting area, following which they were administered either VRET or IP intervention.

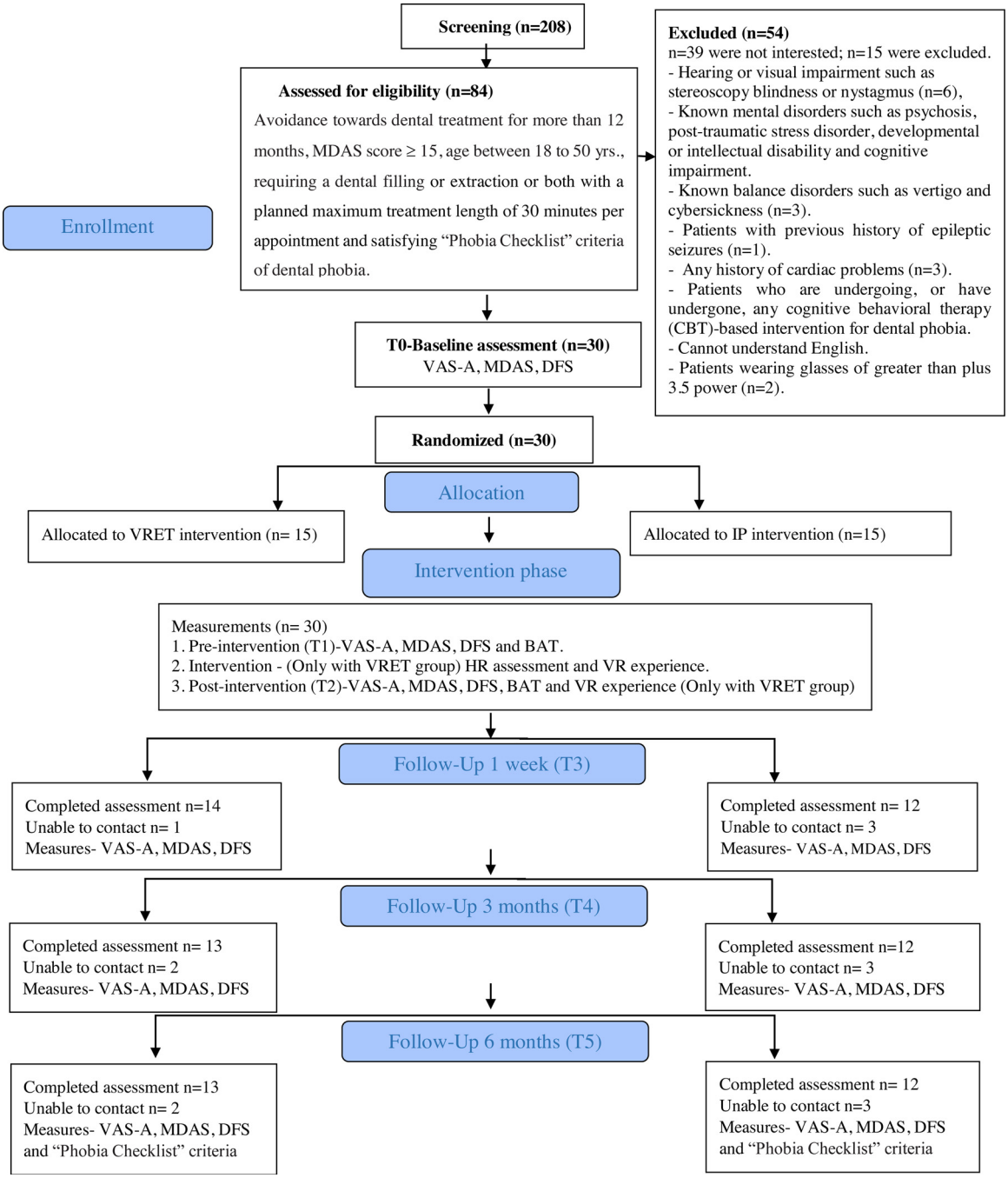

Fig. 1. CONSORT flowchart for the study.

2.3.1. VRET

VRET was conducted utilizing two network computers of which the VR-simulator computer (Dell XPS-8700 desktop with 4th Generation Intel Core i7-4790 processor (8 M Cache, up to 4.0 GHz) and ASUS NVIDIA GEFORCE GTX 750 TI OC 2GB GDDR5 graphic card) rendered the virtual environment and the other user interface-computer allowed the researcher to control and individualize the VR stimuli presented to the patient. An Oculus development kit 2 HMD (Head Mounted Display) with a resolution of 960 × 1080 per eye was used to immerse the participants in the VR dental environment.

Patients in the VRET condition received a single session, multiple scenario VRET, while seated in a dental chair. A two minutes break was provided to the patients at every ten-minute interval to avoid cybersickness. To enhance immersion, typical dental operatory related odour was recreated by placing cotton wool soaked in clove oil around the dental chair. Patients were exposed to five different researcher-controlled VR dental scenarios, using two networked computers and a head mounted device (HMD). A HR wristband (Mio Link) was used to record the physiologic response during and following VRET. VRET intervention included the following three consecutive phases, during which the HR was monitored concurrently:

2.3.1.1. Baseline phase. Patients' baseline HRs were recorded with no VR display in the HMD for 10 minutes.

2.3.1.2. Training phase. Through the HMD, patients viewed a 3-dimensional (3D), stereoscopic, simulated dental operatory for two minutes. Patients could see their own virtual counterpart seated in a

dental chair and look around the dental operatory through the HMD by moving their head.

2.3.1.3. Experimental phase. Patients were exposed to five different VR scenarios (VR1 to VR5), in the following predetermined hierarchy:

a VR1. Dental operatory with dental instruments surrounding the chair and a virtual dentist sitting on the right side of the patient.
b VR2. Virtual dentist moves towards the patient with a dental mirror in the hand, seemingly to do an oral examination.
c VR3. Virtual dentist holds a dental syringe and moves towards the patient.
d VR4. Virtual dentist carries a drill (without sound) towards the patient.
e VR5. Virtual dentist carries a drill (with sound) towards the patient.

The purpose for selecting the above VR scenarios was to gradually assist the patient confront a hierarchy of common anxiety provoking stimuli in the dental setting (Oosterink et al., 2008). Each VR scenario was repeatedly presented to the patient until a change in distress score of ≤ 2 was obtained, after which the next scenario was introduced. Patients were encouraged to keep their mouth open from VR2 through VR5. Still pictures of all the VR scenarios can be found in the case study published earlier (Gujjar et al., 2017). Total duration of VRET was noted for each patient. For the study, the VRET session was planned to be conducted in a single visit. However, if patients were unable to face all the scenarios in a single visit (for example, asking to stop VRET due to excessive fear) they were scheduled for additional appointments to complete VRET and were excluded from the study.

2.3.1.4. Immediate post-VRET phase. Patients completed a series of self-reported measures questionnaires (Raghav et al., 2016). HR was recorded for 10 minutes following the conclusion of VRET.

2.3.2. Informational pamphlet

Patients in the IP condition received a pamphlet containing standard information about overcoming dental anxiety (Heaton, Leroux, Ruff, & Coldwell, 2013). They were seated in the dental chair in the dental clinic and were allowed sufficient time (up to 45 minutes) to review the pamphlet and ask questions related to their dental anxiety.

After the interventions (T2), patients from both intervention groups completed questionnaires indexing state anxiety and dental trait anxiety. Patients from VRET condition also completed VR experience questionnaire.

2.4. Outcome measures

2.4.1. Primary outcome measure

State anxiety was measured using VAS-A (Luyk, Beck, & Weaver, 1988), while dental trait anxiety was evaluated using the original validated MDAS (Humphris et al., 1995) and the DFS (Kleinknecht, Klepac, & Alexander, 1973). All questionnaires were in English. Both state anxiety and dental trait anxiety were indexed at T0, T1, T2, T3, T4 and T5.

2.4.2. Secondary outcome measures

2.4.2.1. Behavioral avoidance test (BAT). BAT was performed at T1 and T2 for both VRET and IP conditions. During this test, patients were exposed to five real dental situations (steps) and asked to rate their level of anxiety for each, on a scale of 0–10 (Doering, Ohlmeier, de Jongh, Hofmann, & Bisping, 2013). The dental situations included a) sitting in the dental chair, b) getting oral cavity examined using dental mirrors, c) watching an approaching dental syringe, d) watching an approaching dental drill without sound and d) watching an approaching dental drill with sound. To measure the ability of patients to tolerate the situation/s, the number of steps completed successfully were also noted (Doering et al., 2013).

2.4.2.2. HR response. A Miolink (MioGlobal, U.S) HR wrist band was used to record the HR during and after VRET. The HR wristband was programmed to record the HR in beats per minute.

2.4.2.3. VR experience (presence, realism, cybersickness and distress). Presence, realism and cybersickness were measured after the first exposure with each VR scenario and at T2, using an 11-point Verbal Rating Scale (VRS) (Hoffman et al., 2001) that ranged from 0–10, where 10 represented the peak presence, realism or cybersickness experience.

The intensity of the current distress experienced by the patients following exposure with each VR scenario was determined using a Subjective Unit of Distress Scale (SUDS; (Wolpe, 1969). Each VR scenario was repeatedly presented to the patient until an SUDS score of ≤ 2 was obtained, after which the next higher scenario was introduced. The scores of VR experience were recorded following first exposure with each VR scenario and at post-therapy (except SUDS).

Time perception during VRET was evaluated by asking the patients to guess the approximate duration they thought they spent in the VR environment (Schneider, Kisby, & Flint, 2011).

2.4.2.4. Dental attendance and number of patients who no longer met the diagnostic criteria for dental phobia. The number of patients who had scheduled dental appointment/s before, or at, T5 was recorded by verbally asking the participants whether or not they had made a dental appointment. This self-reported dental attendance of the patients was confirmed by crosschecking their self-report against the entries in patient records in the university clinic. All patients were assessed for presence of dental phobia using the Phobia Checklist (Oosterink et al., 2009) at T0 and T5. Detailed description and chronology of outcome measure assessment are presented in Table 1 (Raghav et al., 2016).

2.5. Sample size estimation

There were limited comparable studies for estimation of sample size owing to the novelty of our trial. We used the results of an independent-samples *t*-test between the experimental and control group of a previous study (Heaton et al., 2013) for sample size estimation with a power of 0.9. Further, we adjusted for any drop-outs at the rate of 15% and at 10% for any crash of the VR software during therapy, getting the final sample size of 30 patients (15 VRET and 15 IP; (Raghav et al., 2016).

2.6. Data analysis

Statistical analysis was performed using SPSS (IBM, version 23, Chicago IL, USA) with alpha set at 0.05 for all analyses. An intention to treat analysis (ITT) was conducted on the data, whereby missing values of a dropped-out patient were replaced with the mean score from the other patients in the same condition.

Primary outcome measures were analyzed using a 6 (T0 through T5) by 2 (VRET and IP) repeated measures MANOVA, with VAS-A, MDAS and DFS as the dependent variables. Possible differences in mean dental anxiety scores between the VRET and IP condition at T0, T1, T2, T3, T4 and T5 were determined using independent-samples t-tests.

The secondary outcome measures (i.e., BAT scores and steps at T1 and T2) were compared within and between the treatment conditions using paired-samples t-tests and independent-samples t-tests respectively. In addition, Cohen's d effect sizes were calculated within and between conditions at different time points (T1-T5). The HR data obtained during and after VRET was expressed as mean HR at baseline phase, training phase, 1st and last exposure (experimental phase) of each VR scenario, and post-VRET phase. Physiological arousal (increase in HR response) was determined by comparing the mean HRs recorded at baseline, training phase and 1st exposure of each VR scenario

Table 1
Description of primary and secondary outcome measures and timing of measurement.

	Measure	Description	Timing
Primary Outcome measures			
1.	Visual analogue scale for anxiety (VAS-A)	VAS-A (Luyk et al., 1988) asks the patient to put a cross mark (X) on a 0–100 mm scale from totally calm (0) and relaxed to worst fear imaginable (100). This measure is regarded as a simple, sensitive, fast, reliable and valid tool in state dental anxiety assessment (Facco et al., 2011).	T0, T1, T2, T3, T4, T5
2.	Modified Dental Anxiety Scale (MDAS)	MDAS (Humphris et al., 1995) comprises of a 5-item scale assessing anticipatory dental anxiety, fear of dental cleanings, drilling, and injections using a 5-point Likert scale. Possible scores range from 5 to 25, with greater scores indicating a higher level of dental anxiety. The MDAS shows a high level of internal consistency and good construct validity (Humphris, Freeman, Campbell, Tuutti, & D'Souza, 2000).	T0, T1, T2, T3, T4, T5
3.	Dental Fear Survey (DFS)	The Dental Fear Survey (DFS; (Kleinknecht et al., 1973) comprises of a 20-item measure to identify the participants' emotional and physiological reactions associated with dentistry, as well as avoidance of dental care. The possible scores range from 20 to 100, with greater scores indicating higher levels of dental anxiety. The DFS proved to be a reliable, valid and sensitive questionnaire (Davis, Ollendick, & Öst, 2012).	T0, T1, T2, T3, T4, T5
4.	Behavioural Avoidance Test (BAT	The Behavioural Avoidance Test (BAT) essentially contained 5 situational steps that occur commonly during a dental visit (e.g. sitting in the dental chair, inspection of the oral cavity using two dental mirrors, approaching dental syringe, approaching dental drill without sound and approaching dental drill with sound). The BAT involves standardized observations of behaviour and an interview for both intervention groups. The patients undergo sequential steps towards their anxious stimuli comparable to the VRET scenarios and provides a baseline behavioral assessment measure to compare the responses of the patient before and after the interventions. Patients are requested to indicate their level of state anxiety on a scale of 0–10 in each situation. To measure whether the patients are able to tolerate the situation/s the number of steps completed are noted. For the purpose of this study both observation and responses to the standardized situations were recorded during the procedure (Doering et al., 2013).	T1, T2
Secondary outcome measures			
1.	Psychophysiological parameter	A HR wrist band was used to continuously record the HR response of the participants during and post VRET.	During VRET and T2
2.	VR experience after VRET	**Presence, realism and cybersickness (severity of nausea)** were measured with an 11-point verbal rating scales (Hoffman et al., 2001)[#]. **Intention to use VR goggles again and to revisit the dental surgery** was measured using a yes/no response.	T2
3.	Dental attendance and dental phobia evaluation.	Dental attendance was evaluated by asking the patients the number of visits they could make within 6 months. Presence of Dental phobia was evaluated with a "Phobia Checklist"	T5

[#]0 = No presence, realism and cybersickness.
1–3 = Mild presence, realism and cybersickness.
4–6 = Moderate presence, realism and cybersickness.
7–9 = Strong presence, realism and cybersickness.
10 = Profound presence, realism and cybersickness.

(experimental phase) using a repeated measures ANOVA. Physiological habituation (decrease in HR response) was indexed using a paired-samples *t*-test to compare the mean HRs of first and last exposure within each VR scenario and the mean HR at baseline with mean HR of post-VRET phase. Repeated measures ANOVA was performed separately for presence, realism and SUDS (distress) scores across time points. Any violations of sphericity were determined using the Mauchly's test. Since the cybersickness scores showed a non-normal distribution, these data were analyzed using the Friedman's test, followed by pairwise comparisons using the Wilcoxon signed-rank test, in case of a significant finding. A χ^2 test was performed to assess the differences in the proportion of patients with no dental phobia in both conditions at T5.

3. Results

The results are reported according to the updated CONSORT 2010 guidelines (Moher et al., 2012).

At T0, no statistically significant differences were found between the VRET and IP conditions with respect to age, gender, state anxiety and dental trait anxiety, implying successful randomization (Table 2). There were four drop-outs (one from VRET and three from IP condition) at T3 and a total of five drop-outs by the end of T4 and T5 (two from VRET and three from IP condition). No significant differences were detected between the outcome measures of the drop-outs and treatment completers, albeit a significantly lower DFS score was noted amongst the drop-outs of the IP condition, compared to the VRET condition.

All VRET patients (n = 15) required a single session and were able to undergo gradual controlled exposure with the five different VR scenarios. The mean duration of VRET sessions was 40.06 minutes (SD = 20.82; range 13–96 minutes). Ratio of mean time perception of patients (M = 30.20, SD = 15.67) to actual mean duration (M = 40.07, SD = 20.82) of the VRET sessions was 0.75.

3.1. Primary outcome measures

The results of the analysis based on ITT did not differ from the results of the analysis based on only treatment completers. Hence, only the results of the ITT analysis are presented here.

3.1.1. State anxiety and dental trait anxiety

In order to compare the multiple mean dental anxiety scores over time in the VRET and IP condition, a repeated measures MANOVA was conducted (see Table 3 for mean scores). Results showed a significant multivariate main effect of time, $F(15, 14) = 4.6$, $p = 0.003$, implying that the mean scores over time were not the same. Subsequent univariate analysis showed that the time effect was present for all dependent variables; VAS-A, $F(5, 140) = 15.3$, $p < 0.001$; MDAS, $F(5, 140) = 30.2$, $p < 0.001$; and the DFS, $F(5, 140) = 23.0$, $p < 0.001$. Next, pairwise comparisons showed a similar effect for all dependent variables. From T0 to T1, no significant differences in the mean anxiety scores were evident, while from T1 to T2, statistical significant reductions in mean anxiety scores were found. From T2 to T5, the mean scores were either stable or decreased only slightly.

More interestingly, a significant multivariate interaction effect between time and condition was found, $F(15, 14) = 3.3$, $p = 0.015$, implying that not all changes over time were the same for both

Table 2
Comparison of baseline demographic, state and trait anxiety scores between the Virtual Reality Exposure Therapy (VRET) and Informational Pamphlet (IP) condition.

Variables	VRET group (n = 15)	IP group (n = 15)	Test result	d#
Age	25.3(8.6)^	23 (8.9)	t (28) = 0.70; p > 0.05	–
Sex	7 male;8 female	5 male;10 female	χ^2 (1) = 0.55; p > 0.05	–
T0-VAS[a]	70.3(14.2)	68(9.8)	t (28) = 0.52; p > 0.05	0.19
T0-MDAS[b]	18.8(2.8)	18.3(2.6)	t (28) = 0.46; p > 0.05	0.19
T0-DFS[c]	64.8(5.7)	63.8(9.3)	t (28) = 0.35; p > 0.05	0.13

^Mean score, standard deviations (in parentheses); d#, effect size reported as absolute values.
[a] VAS-A score ranges from 0–100; greater score indicates higher state anxiety.
[b] MDAS possible score ranges from 5–25; greater score indicates higher dental trait anxiety.
[c] DFS possible score ranges from 20–100; greater score indicates higher dental trait anxiety.

conditions. Subsequent univariate analysis showed that the interaction effect was present for all dependent variables; VAS-A, F (5, 140) = 12.7, p < 0.001; MDAS, F (5, 140) = 18.5, p < 0.001; and DFS, F (5, 140) = 23.1, p < 0.001. Subsequent pairwise comparisons showed a similar effect for all dependent variables. For the VRET condition, the mean anxiety scores decreased significantly from T1 to T2, and were stable across the other time points, whereas the mean anxiety scores in the IP group remained stable throughout all time points. The interaction effects for the dependent variables are illustrated in Figs. 2–4. As can be seen in Table 3, following the intervention, state and dental trait anxiety scores differed significantly between the conditions at T2, T3, T4 and T5 with large effect sizes (Cohen's d > 0.8) favoring the VRET condition.

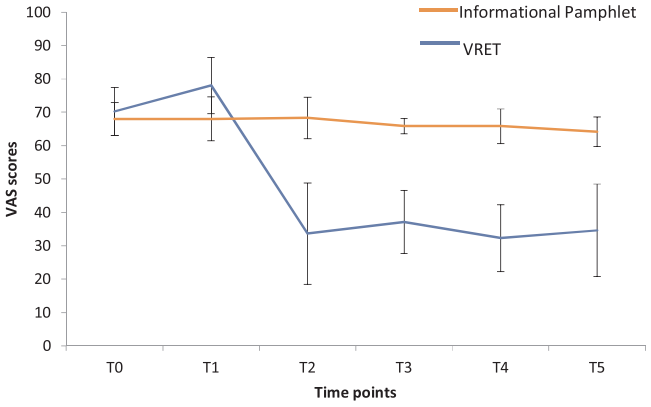

Fig. 2. Mean VAS scores with 95% C.I. at each time point, for the IP and VRET condition.

3.2. Secondary outcome measures

3.2.1. Behavioral avoidance

Paired-samples t-tests within condition revealed statistically significant differences between pre and post intervention BAT scores [t (14) = 8.09; p < 0.01] and the number of steps patients could tolerate [t (14) = −7.36, p < 0.001]. Cohen's *d* effect sizes for BAT scores and BAT steps were larger in the VRET condition (1.24 and 1.33 respectively) compared to the IP condition (0.44 and 0.48 respectively)

With respect to between condition BAT scores and steps at T2, independent-samples t-tests revealed a significantly lower mean BAT score and a significantly greater number of steps tolerated by the patients in the VRET condition compared to the IP condition (see Table 3)

3.2.2. Heart rate

A significant difference was found between the means of HR recorded at baseline, training phase and first exposure of each VR scenario [F (3.3, 46.8) = 3.27, p < 0.05]. A downward trend was observed for mean HRs of first exposures from scenario VR1 through VR5. Although none of the comparisons between the mean HRs of 1st and the last exposure within each VR scenario yielded a significant difference, mean post-VRET HR was significantly lower than the mean baseline HR [t (14) = 2.25, p < 0.05].

3.2.3. VR experience (presence, realism, cybersickness and distress)

The Mauchly's test showed no violation of sphericity regarding presence, realism and distress scores (all p's > 0.05). As seen in Table 4, separate comparisons for presence and realism scores at different time points of VRET (from VR1 through post-VRET) showed no significant differences, indicating that the patients experienced a consistent

Table 3
Comparison between Virtual Reality Exposure Therapy (VRET) and Informational Pamphlet (IP) condition on mean state and dental trait anxiety scores, Behavioral Avoidance Test (BAT) scores and BAT steps, at different time points.

	T1			T2			T3			T4			T5		
	VRET Mean (SD)	IP Mean (SD)	d	VRET Mean (SD)	IP Mean(SD)	d	VRET Mean(SD)	IP Mean(SD)	d	VRET Mean(SD)	IP Mean(SD)	d	VRET Mean(SD)	IP Mean(SD)	d
VAS[a]	78.0(16.6)	68.0(12.9)	0.67	33.6(30)	68.3(12.1)	1.52*	37.1(18.6)	65.8(4.5)	2.12*	32.3(19.6)	65.8(10.3)	2.14*	34.6(27.4)	64.1(8.8)	1.45*
MDAS[b]	20.0(3.4)	17.8(2.1)	0.78	12.9(4.2)	18.2(1.9)	1.63*	11.8(3.7)	17.5(1.5)	2.02*	11.2(3.3)	17.0(1.4)	2.29*	10.0(4.6)	16.4(3.1)	1.63*
DFS[c]	68.0(7.8)	64.4(12.1)	0.35	46.8(11.5)	66.2(11.3)	1.70*	41.6(12.8)	65.7(6.1)	2.40*	38.5(13.6)	63.9(6.8)	2.36*	38.0(17.3)	61.9(7.5)	1.79*
BAT[d]	38.4(4.5)	33.4(2.8)	1.33*	21.8(8.0)	32.7(2.2)	1.86*									
BAT Steps[e]	2.1(0.3)	2.2(0.4)	0.28	3.5(0.6)	2.4(0.6)	1.83*									

[a] VAS-A score ranges from 0–100; greater score indicates higher state anxiety.
[b] MDAS possible score ranges from 5–25; greater score indicates higher dental trait anxiety.
[c] FS possible score ranges from 20–100; greater score indicates higher dental trait anxiety.
[d] BAT possible score ranges from 5–50; greater score indicates higher avoidance.
[e] BAT steps possible score ranges from 1–5; greater score indicates lower avoidance.
* p < 0.05; d, effect size reported as absolute values; VRET, Virtual Reality Exposure Therapy; IP, Informational Pamphlet; T1, pre-intervention; T2, post-intervention; T3, 1 week follow-up; T4, 3 months follow-up; T5, 6 months follow-up.

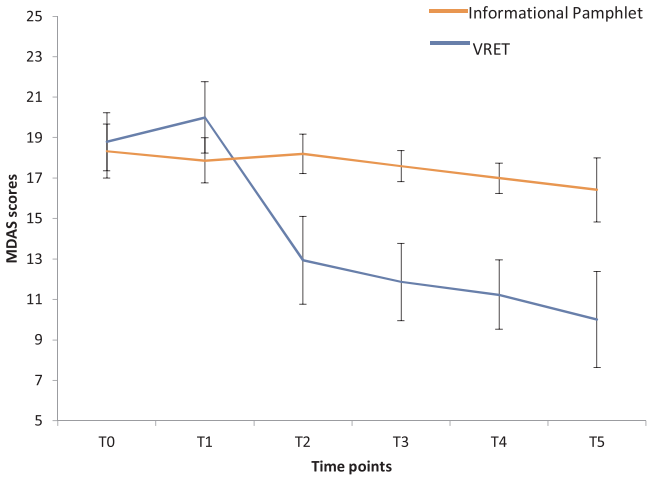

Fig. 3. Mean MDAS scores with 95% C.I. at each time point, for the IP and VRET condition.

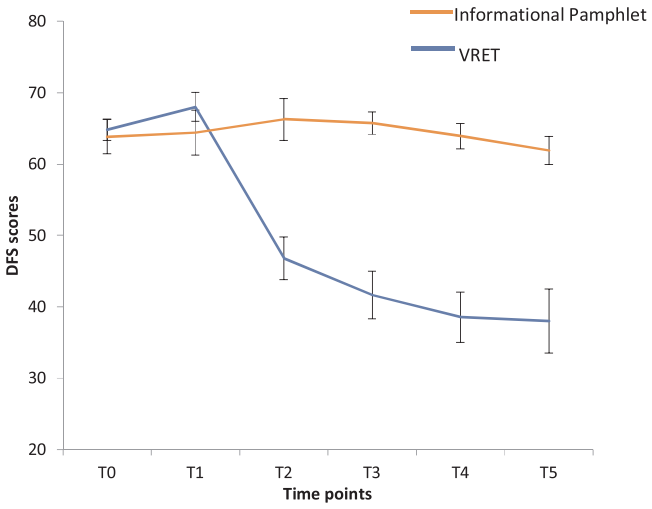

Fig. 4. Mean DFS scores with 95% C.I. at each time point, for the IP and VRET condition.

presence and realism throughout the VRET. However, significant differences were noted for the in-between comparisons of means of distress scores from VR1 through VR5 [F (4, 56) = 3.98, p < 0.01]. Additionally, pairwise in-between comparisons of distress scores from VR1 through VR5 revealed significant differences (all ps < 0.05) between pairs of distress scores measured at VR 1 and VR 3, VR 1 and VR 5, VR 2 and VR 3, VR 2 and VR 5, VR 3 and VR4, VR4 and VR5, implying a gradual increase in level of distress with the introduction of VR3, VR4 and VR5.

The Friedman test showed a statistically significant difference between the mean ranks of cybersickness scores measured at various time points (Table 4). Wilcoxon signed-rank tests showed significant differences when cybersickness scores at post-VRET were compared with the cybersickness scores at VR2, VR4 and VR5. An increase in mean cybersickness score was evident at post-VRET.

3.2.4. Dental attendance

A total of 16 patients, i.e., 10 (77%) from the VRET condition, and 6 (50%) from the IP condition [χ^2 (1) = 1.99; p > 0.05] scheduled an appointment for dental treatment and underwent actual dental treatment within 6 months following the intervention.

3.2.5. Number of patients no longer fulfilling the diagnostic criteria of dental phobia

Of the 25 treatment completers, 11 (85%) from the VRET condition, and 2 (17%) from the IP condition [χ^2 (1) = 11.54; p < 0.001], did not fulfill the criteria of specific (i.e., dental) phobia at 6-month follow-up.

4. Discussion

The results of this study support our hypothesis that VRET would be associated with a significantly greater decrease in dental anxiety and behavioral avoidance compared to those who received IP as intervention. The findings of the self-reported measures are corroborated by the fact that a large proportion of VRET patients underwent actual dental treatment relative to the control condition, within six months following the intervention. Superiority of VRET over the control condition was also underlined by the finding that at 6-month follow-up, a significantly greater proportion of the treatment completers in the VRET condition than in the IP condition did not fulfill the criteria of dental phobia anymore. This suggests that the VRET as applied in the present study was efficacious in the treatment of dental phobia.

The positive effects of VRET could partly be attributed to the strong presence and realistic VR experience perceived by the patients throughout the therapy. It has been found that controlled and realistic visual, olfactory and auditory cues (Maples-Keller, Yasinski, Manjin, & Rothbaum, 2017) during VRET activate the underlying fear structure (Price, Mehta, Tone, & Anderson, 2011). Additionally, exposure optimization strategies applied in our study such as prolonged, focused and controlled confrontations with patients' feared stimuli in the absence of aversive outcome (Rothbaum, Hodges, Smith, Lee, & Price, 2000) may have resulted in a reduction of the fear response (Craske et al., 2014) in the patients.

Physiological habituation was evident post-VRET, implying successful exposure therapy using virtual reality (Diemer, Muhlberger, Pauli, & Zwanzger, 2014). Although HR is regarded as the most potent physiological anxiety measure in patients with specific-phobias, dissonance was observed between different measures of anxiety (Wilhelm et al., 2005). That is, while progressing to a higher anxiety provoking VR scenario/stimuli for e.g. VR3, VR4 and VR5 resulted in more distress experienced by the patients (higher SUDS score), HR (from scenario VR1 through VR5) showed a downward trend. This is consistent with Fowles' motivational theory which predicts that VRET specifically activates the behavioral inhibitory system, thereby causing a reduction in HR (Wilhelm et al., 2005). Also, the focused visual attention of the

Table 4
Comparison of mean (SD) presence, realism and cybersickness scores within the Virtual Reality Exposure Therapy (VRET) condition at different time points.

	VR1		VR2		VR3		VR4		VR5		Post-VRET		
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Test result
Presence	6.80	2.59	6.93	2.01	7.26	2.28	6.20	2.85	7.80	1.93	7.33	1.71	F (5,70) = 1.62, p > 0.05[a]
Realism	6.33	2.12	7.26	1.62	7.40	2.19	6.66	2.38	7.60	2.13	7.13	2.06	F (5,70) = 1.77, p > 0.05[a]
Cybersickness	.66	1.63	.53	1.59	.66	1.49	.60	1.68	.46	1.80	1.66	2.43	χ^2(5) = 14.12, p < 0.05*

VR1 = Virtual Reality scenario 1, VR2 = Virtual Reality scenario 2, VR3 = Virtual Reality scenario 3, VR4 = Virtual Reality scenario 4, VR5 = Virtual Reality scenario 5, VRET = Virtual Reality Exposure Therapy; [a] Repeated Measures ANOVA, * Friedman test.

patients might have led to activation of cardiac parasympathetic activity and a reduced cardiovascular response (Wilhelm et al., 2005). In order to objectively evaluate the treatment outcomes, and to better understand the underlying mechanisms during VRET, future research could use more sensitive psychophysiological measures such as heart rate variability and skin conductance response.

The present study has several limitations that should be noted. Firstly, we could not blind the patients or the therapist to the interventions due to the apparent differences between the two interventions. However, data files containing data from different conditions were sent as separate files to the data analyst (AVW) with the patient identifiers in the data files blinded (Karanicolas, Farrokhyar, & Bhandari, 2010). Secondly, we compared VRET with a non-active IP control condition. The choice for this control was based upon the fact that informational pamphlets are commonly used by dental practitioners due to their ease of administration. Yet, in future studies it might be useful to compare VRET with an active control such as *in vivo* exposure therapy due to greater likelihood of it providing a better estimate of the effectiveness of VRET. Thirdly, the fact that we used a sample of dental phobia patients who visited an out-patient clinic, may be considered a limitation for the generalizability of the study findings since a large number of patients with a dental phobia avoid dental offices. However, the large effect sizes that were obtained supports testing of VRET as a remote therapy in patients with dental phobia with total avoidance towards dental treatment. Fourthly, the VRET used in this study contained only five (albeit most commonly encountered) dental scenarios with all patients exposed to the same five VR scenarios. Although this was done for reasons of consistency and standardization of the intervention, it may be considered a limitation because the stimuli that trigger dental anxiety may differ for each individual (Oosterink et al., 2008). Therefore, conducting future studies in VRET using additional VR sounds and scenarios such as dental aspirator sounds, root canal and dental scaling sounds and instruments would make VRET relevant to more individuals. Fifthly, the VRET program used a caucasoid male dentist avatar, while the patient population was largely multiethnic Malaysian. Nonetheless, regardless of the sex and race of the dentist avatar, the VRET device used in the present study was able to trigger a significant fear response in patients. It would be interesting to study the effects of using VRET programs that provide option of selecting race and sex of the dentist avatar. Finally, patients experienced mild cybersickness post-VRET. However, severity of cybersickness experienced during the present study was less than what was observed during the feasibility study (Gujjar et al., 2018), possibly because more breaks were provided during the present RCT compared to the feasibility study.

5. Conclusion

The results of this study provide evidence to support the efficacy of VRET in the treatment of dental phobia. Also, the positive findings in relation to both subjective and objective measures support using VRET in routine dental practice.

Author's contribution

KRG and ADJ conceptualized the idea. KRG gave therapy to the patients assisted by RK. KRG wrote the initial draft. ADJ and AVW participated in the design and contributed to the statistical analysis. All the authors read the draft, provided feedback and approved the final manuscript. KRG is the guarantor of the paper.

Competing interests

There are no known conflicts of interest associated with this publication.

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