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Feasibility and dissemination of a computerized home-based treatment for Generalized Anxiety Disorder: A randomized clinical trial

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ABSTRACT

Generalized Anxiety Disorder (GAD) is a prevalent, impairing, and undertreated psychiatric disorder. We examined if a home-based computerized treatment program can feasibly be delivered and successfully treat GAD symptoms. Using a randomized control trial, we compared three active groups receiving computerized sequenced Attention Bias Modification (ABM) followed by Applied Relaxation psychoeducation (AR-pe), the reversed sequence of AR-pe and ABM, and a simultaneous ABM and AR-pe group to an assessment only control group. The participants comprised 169 adults with a diagnosis of GAD. We asked participants to complete as many as twenty-four 30-min sessions of an at-home computerized treatment program over 12 weeks. The control group received 24 brief assessment questionnaires as well as assessments of attention bias. Results from intent-to-treat analyses show faster rate of improvement for symptoms of anxiety as measured by the Hamilton Anxiety Rating Scale (HAM-A) over time in groups that received active training in contrast to the clinical monitoring (CM) control group. Follow-up analyses revealed that both sequenced groups improved in anxiety when compared to the control group, while the simultaneous group did not outperform the control group. Results suggest that sequenced delivery of ABM and AR, may be a viable home-based treatment option for individuals with GAD who have limited access to resources or are otherwise unable to seek available treatments that require engagement outside of the home.
Trial registration: clinicaltrial. gov Identifier: NCT00602563.

1. Introduction

Generalized anxiety disorder (GAD) is characterized by excessive, uncontrollable, and often irrational worry, with a chronic and unremitting course (APA, 2013; Wittchen & Hoyer, 2001). GAD has a high estimated lifetime prevalence, ranging from 5.7 to 8.5% in primary care settings (Kessler, Berglund, et al., 2005; Kessler, Brandenburg, et al., 2005). Furthermore, GAD is associated with low quality of life, poor perceived health, and high burden on the medical system, resulting in both economic and public health hardship (Wittchen, 2002).

1.1. Dissemination efforts for treating GAD

Although empirically-supported treatments (ESTs) exist for GAD, their availability is limited and is often delayed (Borkovec & Ruscio, 2001; Gunter & Whittal, 2010; Wang et al., 2005). Yearly estimates show that approximately 70% of people with anxiety disorders go untreated (Lépine, 2002). Furthermore, the deployment of ESTs, namely Cognitive-Behavioral Therapy (CBT), is often faced with fidelity and acceptability obstacles that hinder effectiveness in the community (Gunter & Whittal, 2010). Indeed, several individual, provider, and systemic factors act as barriers to treatment. For example, lack of time for engaging in treatment, limited patient and physician access to mental health services, and low rates of training in evidence-based care in mental health services may all contribute to poor access to care (Collins, Westra, Dozois, & Burns, 2004). Thus, there is a need to develop and improve access to cost-effective and easily deliverable effective treatments for GAD.

Dissemination efforts in anxiety disorders have focused on feasibility and improving access through remote means. For example, ESTs for anxiety disorders via computerized programs show promise demonstrating consistent efficacy in randomized controlled trials (RCTs) and primary care settings (Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Craske et al., 2009). However, few studies have examined the efficacy of computer-delivered home-based treatments for GAD.

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1.2. Empirically supported treatments for GAD

Attention bias modification (ABM) is a potentially cost-effective and readily deliverable treatment bridging the above gap (Hakamata et al., 2010). Consistent with cognitive theories of anxiety positing selective attention to threat-relevant information as a maintaining factor for anxiety, ABM comprises a computer-based task to guide attention away from threat-relevant cues; (Amir, Beard, Burns, & Bomyea, 2009; Amir & Taylor, 2012). However, its effectiveness in other clinical populations has yielded mixed results. Moreover, clinical studies have mainly comprised small samples (MacLeod & Clarke, 2015). Finally, of the seven studies that have included location (e.g. at-home versus in lab setting) as a moderator for ABM efficacy in other than anxious populations, five have demonstrated larger effects in the laboratory when compared to remote administration (Cristea, Kok, & Cuijpers, 2015; Heeren, Mogoaş;e, Philippot, & McNally, 2015; Kampmann, Emmelkamp, & Morina, 2016; Linetzky, Pergamin-Hight, Pine, & Bar-Haim, 2015; Price et al., 2016), with the remaining finding no difference (Cristea, Kok, & Cuijpers, 2016; Mogoaşe, David, & Koster, 2014). Thus, there is a need to study further the efficacy of disseminating ABM at home in patients with GAD.

Applied relaxation (AR) is another established EST for GAD, both as a standalone and additive treatment (Borkovec & Costello, 1993; Öst & Breitholtz, 2000). Nonetheless, there is a need to modify AR into more deliverable means. Computer delivered AR plus psychoeducation (AR-pe) has comparable efficiency to therapist-delivered CBT (Andrews et al., 2010). Despite the demonstrated efficacy of therapist-delivered AR-pe for GAD, few studies have examined its efficacy as a home-delivered EST for GAD that can bridge the availability to implementation gap.

1.3. Current study

The current trial examined the feasibility and effectiveness of a home-based computerized treatment using sequenced or simultaneous ABM and AR-pe in individuals diagnosed with GAD. We report the main findings described on clinicaltrials.gov predicting that individuals with GAD completing ABM and AR-pe would improve in symptoms when compared to a clinical monitoring (CM) assessment-only control group.

2. Methods

We recruited adults (age 18–65) between July , 2010 and February 2016 (see CONSORT chart, Fig. 1). Participants completed the intake process over one to three days depending on participant schedule. We recruited participants through advertisement in newspapers, flyers, and radio announcements. Participants were eligible for the study if they met *Structured Clinical Interview for DSM-IV* diagnostic criteria for a primary diagnosis of current GAD (APA, 2000). Exclusion criteria included current treatment (e.g., psychotropic medication or CBT) for GAD initiated less than 3 months prior to the intake, diagnosis of bipolar disorder, schizophrenia, or substance use disorder. Participants who were receiving current treatment were required to be stable on their symptoms and medication. After the intake assessment, participants were randomized into one of the 4 groups: 2 sequenced groups (ABM first followed by AR-pe, AR-pe first followed by ABM), a simultaneous ABM and AR-pe group, or CM group. For clarity, sequenced groups will be referred to as the ABM group and AR-pe group.

2.1. Procedures

2.1.1. Attention Bias Modification Program (ABM)

The ABM program was designed to disengage attention from ideographically selected threatening stimuli using a probe detection task described in previous research (Amir et al., 2009). Each ABM session comprised 288 Threat-Neutral Word Pairs: 2 (Probe Type: E or F) x 2 (Probe Location: Top or Bottom) x 12 (Word pairs) x 6 (Repetitions). Each participant generated 13 GAD-related threat words (e.g., bankrupt, stupid) to be used in the ABM task with the help of a clinician after the intake assessment. From this list we selected 12 distressing words that were then rated using a −3 (very distressing) to +3 (very pleasant) Likert scale. Participants also rated 24 preselected neutral words (e.g., chair) used in previous research (Amir et al., 2009; MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002). From the list of neutral words, we selected 12 with an emotional rating of 0 matched by approximate character length to the threat words.

2.1.2. Applied relaxation plus psychoeducation. (AR-pe)

The AR-pe program comprised 12 modules based on previous computer-delivered programs for anxiety (Andersson, Strömgren, Ström, & Lyttkens, 2002; Ström, Pettersson, & Andersson, 2000; Zetterqvist, Maanmies, Ström, & Andersson, 2003). Twelve videos delivered by an actor provided psychoeducation about contemporary models of anxiety. The videos were 7 min in length on average and comprised the following: general psychoeducation (three modules); the effect of thoughts on emotions (three modules); the utility of exposure (three modules), the utility of breathing and relaxation followed by audio-directed relaxation (one module), the utility of volunteering and giving back to the community followed by audio-directed relaxation (one module), and a review of previously learned lessons from all of the modules as well as guidance on relapse prevention, followed by audio-directed relaxation (one module). Each audio-directed relaxation exercise was approximately 30 min in length script that guided participants through standard progressive muscle relaxation techniques (Marks, Lovell, Noshirvani, Livanou, & Thrasher, 1998).

2.1.3. Condition assignment

We randomized participants to one of the four groups described above. The PI and the project coordinator used a spreadsheet to generate a random number sequence that was then used for assigning groups and codes to participants. Research assistants, and independent accessors were thus blind to condition. At the 3-month follow up assessment, the blind was broken by the interviewers who informed participants whether they were in one of the active conditions or the CM group.

In the three active groups, all participants received both ABM and AR-pe either sequentially or simultaneously. Participants assigned to the CM condition completed computerized assessments for up to 24 sessions. At the end of the intake, participants were provided with a USB drive with a computer program comprising the tasks they were assigned to and instructed in the lab as to how to use the program. We asked participants to complete two sessions of the program every week for the next six weeks. At the end of the six weeks, they were invited to the lab for a second assessment and mid-treatment session. At the mid-treatment session, the treatment sequence was reversed for participants in sequenced arms. Those in the simultaneous and CM groups continued their respective arms after the mid-treatment assessment. In aggregate, all participants were expected to complete up to 24 sessions (twice weekly for 12 weeks) of the program at home.

2.1.4. In-clinic assessments

Post-doctoral fellows, graduate students, and the study principal investigator conducted clinical interviews at all assessments. We invited our participants back to the lab approximately 3-months, 6-months, and 12-months post-completion of the study to complete follow-up interviews. Consensus diagnoses were determined following standardized protocols used in our research clinic involving weekly meetings with senior staff (Amir et al., 2009).

2.2. Measures

Self-report measures: Participants completed a demographic

[a]ABM = Attention Bias Modification, AR-pe = Applied relaxation plus psychoeducation, CM = clinical monitoring.
[b]ABM refers to ABM first followed by AR-pe group, AR-pe refers to AR-pe first followed by ABM group, ABM+AR-pe refers to the simultaneous group, CM refers to the clinical monitoring group.

Fig. 1. CONSORT chart detailing study flow of participants from screening to analysis.
[a]ABM = Attention Bias Modification, AR-pe = Applied relaxation plus psychoeducation, CM = clinical monitoring.
[b]ABM refers to ABM first followed by AR-pe group, AR-pe refers to AR-pe first followed by ABM group, ABM + AR-pe refers to the simultaneous group, CM refers to the clinical monitoring group.

questionnaire as well as the *Penn State Worry Questionnaire* (*PSWQ*; Meyer, Miller, Metzger, & Borkovec, 1990), the state version of the *Spielberger State-Trait Anxiety Inventory* (*STAI-S*; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983),and the *Beck Depression Inventory* (*BDI*) (see Table 1).

Interview measures: We used the *Structured Clinical Interview for DSM-IV-TR Axis I Disorders - Patient Edition (SCID-I-I/P)* to assess eligibility at baseline and subsequently to asses for a continuing diagnosis of GAD and assessed anxiety symptoms by administering the *Hamilton Anxiety Rating Scale* (*HAM-A*; First, Spitzer, Gibbon, & William, 1992; Hamilton, 1969). The *Sheehan Disability Scale* (SDS) was administered to assess current level of interference in daily life due to GAD (Sheehan, 1983). Descriptive statistics for every measure on each time point are presented on Table 2.

2.3. Statistical methods and data analytical plan

The primary registered outcome of the trial was improvement on severity of anxiety symptoms as measured by HAM-A scores. Secondary outcomes included the PSWQ, SDS, BDI, and STAI-S. We used an intent-to-treat with no imputation multilevel longitudinal data analytic strategy, modeling scores of each participant at each assessment as a level one variable (Chakraborty & Gu, 2009). We then used the slope and intercept of each subject's data in level two and used group to predict the slopes and intercepts for each dependent measure (Singer & Willett, 2003).

The analyses using linear mixed effects accounts for missing-values at all time-points (Little & Yau, 1996). The mixed model and intent-to-treat approach has a number of strengths: (1) it can accommodate missing data points in longitudinal datasets; (2) the approach does not need to have the same number of observations per subject; and (3) time can be continuous, rather than a fixed set of points; among other strengths. To analyze clinical improvement, we contrast coded the grouping variable comparing those receiving an active treatment (referred to as active) versus those in the CM condition (referred to as control). Follow-up contrasts analyses compared each active group to

Table 1
Baseline demographic statistics.[a].

Group[b]	Age			Education			Female	Male	Non-White	White
	n	M	(SD)	*n*	M	(SD)	*n*	*n*	*n*	*n*
Total	*169*	38.17	12.74	167	15.58	2.53	*115*	*54*	*57*	*112*
ABM	*45*	39.78	13.81	44	15.25	2.55	*28*	*17*	*13*	*32*
AR-pe	*40*	41.73	11.58	39	16.08	2.61	*27*	*13*	*14*	*26*
ABM + AR-pe	*38*	36.00	12.71	38	16	2.67	*28*	*10*	*13*	*25*
CM	*46*	35.28	11.99	46	15.13	2.27	*32*	*14*	*17*	*29*

[a] ABM = Attention Bias Modification, AR-pe = Applied relaxation plus psychoeducation, CM = clinical monitoring.
[b] ABM refers to ABM first followed by AR-pe group, AR-pe refers to AR-pe first followed by ABM group, ABM + AR-pe refers to the simultaneous group, CM refers to the clinical monitoring group.

the control condition (Rosnow & Rosenthal, 1996). For all models, we treated time as a random factor and compared the same models with time as a fixed factor. In each model we included time as either a fixed factor or a random factor (Singer & Willett, 2003). The models with time as random factor had a better fit to the data than the models with time as a fixed factor. Thus, we modeled time as a random factor and group as a fixed factor in all analyses. We assessed the effect of condition on primary and secondary outcome scores via hierarchical linear mixed effects regression using the lme4 package in R (Version 3.4.1; Bates, Maechler, Bolker, & Walker, 2014) and conducted corresponding power analyses using the nlmeU package (Gałecki & Burzykowski, 2013). Power was calculated based on all the model parameters. Our model comparing HAM-A between active and control groups over time achieved a power of 0.82. For the remaining analysis our average power was 0.69, ranging from 0.42 to 0.85. Results for linear mixed effects are presented on Table 3 and Fig. 2.

3. Results

3.1. Sample characteristics and retention

At baseline, groups did not differ significantly on our primary

Table 2
Descriptive statistics for clinical assessment measures[a,b].

Measure[c]	ABM			ABM + AR-pe			AR-pe			CM		
Time	*n*	M	(SD)	*n*	M	(SD)	*n*	M	(SD)	*n*	M	(SD)
HAM-A												
PRE	*45*	26.71	(7.00)	*38*	26.87	(6.37)	*40*	27.48	(6.90)	*46*	25.28	(6.85)
MID	*28*	17.18	(8.55)	*26*	18.54	(10.01)	*28*	13.61	(6.90)	*27*	20.70	(8.07)
POST	*20*	10.00	(6.16)	*19*	13.63	(9.72)	*25*	8.76	(5.61)	*20*	17.60	(10.66)
3mo	*13*	9.23	(8.63)	*11*	14.09	(7.65)	*22*	8.77	(7.97)	*12*	15.75	(12.34)
6mo	*13*	5.92	(5.28)	*8*	9.25	(7.25)	*11*	5.82	(4.02)	*10*	15.80	(11.94)
12mo	*12*	4.50	(5.63)	*10*	9.40	(7.63)	*12*	7.42	(5.65)	*6*	8.17	(10.55)
PSWQ												
PRE	*45*	69.31	(7.56)	*38*	68.50	(9.91)	*40*	68.53	(10.52)	*46*	70.54	(6.70)
MID	*28*	63.71	(10.89)	*26*	61.00	(12.49)	*28*	60.14	(11.03)	*28*	64.89	(10.43)
POST	*17*	63.18	(11.16)	*21*	58.48	(14.87)	*25*	57.36	(12.41)	*21*	58.95	(15.48)
3mo	*16*	63.69	(17.70)	*11*	54.91	(12.65)	*21*	58.10	(12.43)	*12*	56.00	(16.06)
6mo	*14*	57.86	(12.74)	*8*	56.25	(12.93)	*13*	60.69	(14.75)	*9*	55.67	(12.87)
12mo	*13*	55.69	(12.61)	*11*	54.27	(15.65)	*15*	56.20	(12.44)	*6*	52.17	(20.07)
BDI												
PRE	*45*	27.58	(10.68)	*38*	25.63	(11.67)	*40*	27.45	(10.46)	*46*	29.11	(10.23)
MID	*28*	22.46	(13.62)	*26*	18.38	(11.65)	*28*	15.43	(9.90)	*28*	19.43	(12.75)
POST	*17*	14.82	(10.83)	*21*	19.43	(13.99)	*25*	11.40	(8.78)	*21*	18.48	(14.09)
3mo	*15*	12.93	(11.21)	*11*	11.13	(8.72)	*21*	15.10	(11.54)	*14*	22.57	(15.01)
6mo	*14*	12.21	(13.33)	*8*	16.88	(13.44)	*13*	12.54	(11.11)	*9*	18.89	(12.79)
12mo	*13*	12.08	(12.87)	*11*	12.82	(8.54)	*15*	12.33	(8.93)	*7*	13.29	(12.39)
STAI-S												
PRE	*45*	55.40	(11.27)	*38*	54.76	(10.44)	*40*	53.43	(12.18)	*46*	56.00	(11.12)
MID	*28*	49.68	(12.52)	*26*	45.27	(12.37)	*28*	44.54	(9.52)	*28*	51.50	(12.56)
POST	*18*	46.78	(12.02)	*21*	46.00	(14.67)	*25*	43.16	(9.83)	*21*	42.90	(13.92)
3mo	*16*	42.69	(14.78)	*11*	42.00	(14.44)	*22*	42.50	(11.84)	*13*	46.46	(14.16)
6mo	*14*	44.79	(15.23)	*8*	40.13	(12.91)	*13*	45.38	(13.90)	*10*	46.00	(12.25)
12mo	*13*	39.77	(12.89)	*11*	45.91	(12.51)	*14*	39.07	(6.92)	*6*	36.50	(13.03)
SDS												
PRE	*45*	21.02	(4.38)	*37*	20.05	(4.38)	*40*	21.98	(3.48)	*46*	21.02	(4.38)
MID	*26*	16.04	(6.31)	*26*	14.81	(6.21)	*27*	12.70	(4.77)	*24*	16.88	(6.50)
POST	*18*	11.89	(7.10)	*18*	13.22	(7.01)	*24*	9.71	(5.13)	*18*	15.28	(7.53)
3mo	*13*	10.08	(8.74)	*11*	11.45	(8.71)	*22*	10.09	(6.09)	*12*	15.50	(8.65)
6mo	*13*	6.00	(5.18)	*8*	7.50	(6.59)	*11*	9.73	(2.94)	*11*	11.45	(9.30)
12mo	*12*	5.33	(6.26)	*10*	7.70	(5.33)	*13*	8.00	(5.03)	*5*	8.60	(11.68)

[a] ABM = Attention Bias Modification, AR-pe = Applied relaxation plus psychoeducation, CM = clinical monitoring.
[b] ABM refers to ABM first followed by AR-pe group, AR-pe refers to AR-pe first followed by ABM group, ABM + AR-pe refers to the simultaneous group, CM refers to the clinical monitoring group.
[c] HAM-A = Hamilton Anxiety Rating Scale; PSWQ = Penn State Worry Questionnaire; BDI = Beck Depression Inventory; STAI-S = State-Trait Anxiety Inventory - State; SDS = Sheehan Disability Scale.

Table 3
Linear mixed effect models predicting change in HAM-A by treatment condition[a,b].

Parameter[c]	b	SE	df	*t* or X^2	*p*	*d*
Fixed effects						
Intercept, m_1	27.20	1.39	328	19.53	< .001	4.84
Intercept, m_2	29.38	1.33	160	22.11	< .001	5.89
Intercept, m_3	27.75	1.42	167	19.60	< .001	5.06
Intercept, m4	28.96	1.45	147	19.93	< .001	5.78
Level 1 (participant specific)						
Time, m_1	−2.62	0.51	328	−5.07	< .001	0.47
Time, m_2	−4.67	0.47	160	−9.88	< .001	0.94
Time, m_3	−4.33	0.48	167	−8.94	< .001	0.79
Time, m4	−4.12	0.63	147	−6.57	< .001	0.82
Level 2 (condition-specific)						
Active vs Control, m_1	1.39	1.61	165	0.86	0.392	0.25
ABM first vs Control, m_2	−2.21	1.89	88	−1.17	0.245	0.44
AR-pe first vs Control, m_3	−0.59	1.98	83	−0.30	0.767	0.11
ABM + AR-pe vs Control, m_4	−1.82	1.99	82	−0.91	0.364	0.36
Cross-level interaction						
Time X Active vs Control, m_1	−1.69	0.59	328	−2.87	0.004	0.30
Time X ABM first vs Control, m_2	2.08	0.69	160	−9.88	0.003	0.42
Time X AR-pe first vs Control, m_3	1.72	0.73	167	2.35	0.020	0.31
Time X ABM + AR-pe vs Control, m_4	1.55	0.88	147	1.76	0.081	0.31

[a] ABM = Attention Bias Modification, AR-pe = Applied relaxation plus psychoeducation, CM = clinical monitoring.

[b] ABM refers to ABM first followed by AR-pe group, AR-pe refers to AR-pe first followed by ABM group, ABM + AR-pe refers to the simultaneous group, CM refers to the clinical monitoring group.

[c] m1 = Active (ABM, AR-pe, ABM + AR-pe) vs CM over time; m2 = ABM vs CM over time; m3 = AR-pe vs CM over time; m4 = ABM + AR-pe vs CM over time.

outcome (HAM-A, F (3,165) = 0.82, p = .487) or secondary measures (PSWQ, F (3,165) = 0.53, p = .665; SDS, F (3,164) = 1.73, p = .162; BDI, F (3,165) = 0.73, p = .536; STAI-S, F (3,165) = 0.40, p = .750). Although our primary outcome variable was a continuous measure, we also classified participants as responders on our primary outcome measure defined as HAM-A scores ≤7 at week 13 (Rickels, Rynn, Iyengar, & Duff, 2006). Of the active groups, 26/63 (41%) of participants met remission criteria at the end of week 13 compared to 4/21 (19%) of participants in the CM group. Consistent with intent-to-treat analyses, we retained all observations for any participant for any time point. However, to remain consistent with traditional completer analyses, we define participant dropout attrition, or treatment dropout, to when a participant did not return for the 6-week interview and second sequencing point. The full enrolled and randomized sample of 169 had a dropout attrition of 35.5%, whereas the dropout attrition for the CM, ABM, AR-pe, and simultaneous group was 41.3%, 37.8%, 30.0%, and 31.6% respectively.

3.2. Treatment implementation and service utilization

We asked participants in the sequenced ABM group to complete 12 ABM sessions from baseline to the 6-week mid-assessment, at which point they were asked to complete 12 AR-pe modules. Participants in the sequenced AR-pe group were asked to watch the 12 AR-pe modules from baseline to the 6-week mid-assessment, at which point they were asked to complete 12 ABM sessions. Those in the simultaneous group were asked to complete both 12 AR-pe modules and 12 ABM sessions within a six-week period and were also told to repeat watching the modules and complete the ABM sessions at the mid-assessment session (i.e., told to watch modules and ABM sessions a total of 24 occasions throughout a 12-week period).

We defined non-usage attrition as users who did not engage with treatment content (Donkin et al., 2011), comprising viewing a AR-pe module or completing 1 session of ABM. From the 123 participants who completed the intake and were randomized to an active condition, 108 (87.8%; non-usage attrition of 12.2%) completed at least one full session of the program at home (measured by completing a session of the probe detection task – or 288 trials – at least once or watching at least one video). Non-usage attrition for the ABM task in the active groups was 28.5%, while ABM non-usage attrition for the ABM, AR-pe, and simultaneous groups were 8.9%, 40%, and 39.5% respectively. Non-usage attrition for the video modules in the active groups was 43.1%, while video non-usage attrition for the ABM, AR-pe, and simultaneous group were 60%, 30%, and 36.8% respectively. Non-usage attrition for any audio was 68.3% for all active groups (or AR-pe = 55%, ABM = 73.3%, simultaneous ABM & AR-pe = 76.3%). Only two participants (one in the ABM group and one in the AR-pe group) completed every video and ABM session.

Participants in the ABM group watched a median of 11 (92%) videos; participants in the AR-pe group watched a median of 15 (125%); participants in the simultaneous ABM and AR-pe group watched a median of 10.5 (43.8%; based on 24 sessions) with a median of 9 videos (75%) from baseline to mid-assessment and a median of 6 videos (50%) from mid-assessment to post-assessment. Participants assigned to the sequenced groups were asked to perform the probe detection task for a minimum of 12 sessions (12 X 288 = 3456 trials), whereas those in the simultaneous group were asked to repeat the sessions at the 6-week mid-assessment, for a total of 24 sessions (24 X 288 = 6912 trials). Participants in the ABM group completed a median of 2592 (75.0%) probe detection trials; participants in the AR-pe group completed a median of 2880 (83.3%) probe detection trials; participants in the simultaneous ABM and AR-pe group underwent a median of 2304 (33.3%) probe detection trials, where a median of 1728 (50%) were completed from baseline to mid-assessment and 864 (25%) from mid-assessment to post-assessment.

Chi-square analyses revealed significant differences in engagement in the ABM task between the ABM group and the AR-pe group ($\chi^2(1) = 11.28$, p < .001), and the ABM group and the simultaneous group ($\chi^2(1) = 11.09$, p < .001). There were also between-group differences in engagement in the AR-pe tasks between the AR-pe group and ABM group ($\chi^2(1) = 8.75$, p < .01), but not the AR-pe group and the simultaneous group ($\chi^2(1) = 0.5$, p = .522).

3.3. Clinical outcomes

Using the above described mixed linear model analysis with HAM-A as the dependent variable comparing all active groups versus the control group, there was a significant interaction of Time-by-Condition (b = 1.69, SE = 0.59, df = 328, t = 2.87, p = .004, d = 0.30), with time treated as a random factor and condition treated as a fixed factor. Table 3 presents complete results, and Fig. 2 presents a graphical representation of this interaction. Follow-up analysis comparing the ABM group to the control group also revealed a Time-by-Condition interaction (b = 2.08, SE = 0.69, df = 160, t = 3.001, p = .003, d = 0.42), as did the AR-pe group compared to the control group (b = 1.72, SE = 0.73, df = 167, t = 2.35, p = .020, d = 0.31). The interaction effect when comparing the simultaneous ABM with AR-pe group with the control group, however, was not significant (b = 1.55, SE = 0.88, df = 147, t = 1.76, p = .081, d = 0.31).,[1] [2]

Analyses for the SDS showed a marginally significant Time-by-Condition interaction (active versus control; b = 0.86, SE = 0.44, df = 316, t = 1.94, p = .053, d = 0.21). Follow-up analysis revealed that there was significant Time-by-Condition interaction for the ABM group compared to control (b = 1.27, E = 0.57, df = 151, t = 2.22,

[1] See supplemental materials for Tables & Figures detailing results from Baseline to 6-weeks.

[2] Per a reviewer suggestion, we also conducted follow-up analyses comparing active groups. This analysis did not result in any significant effects.

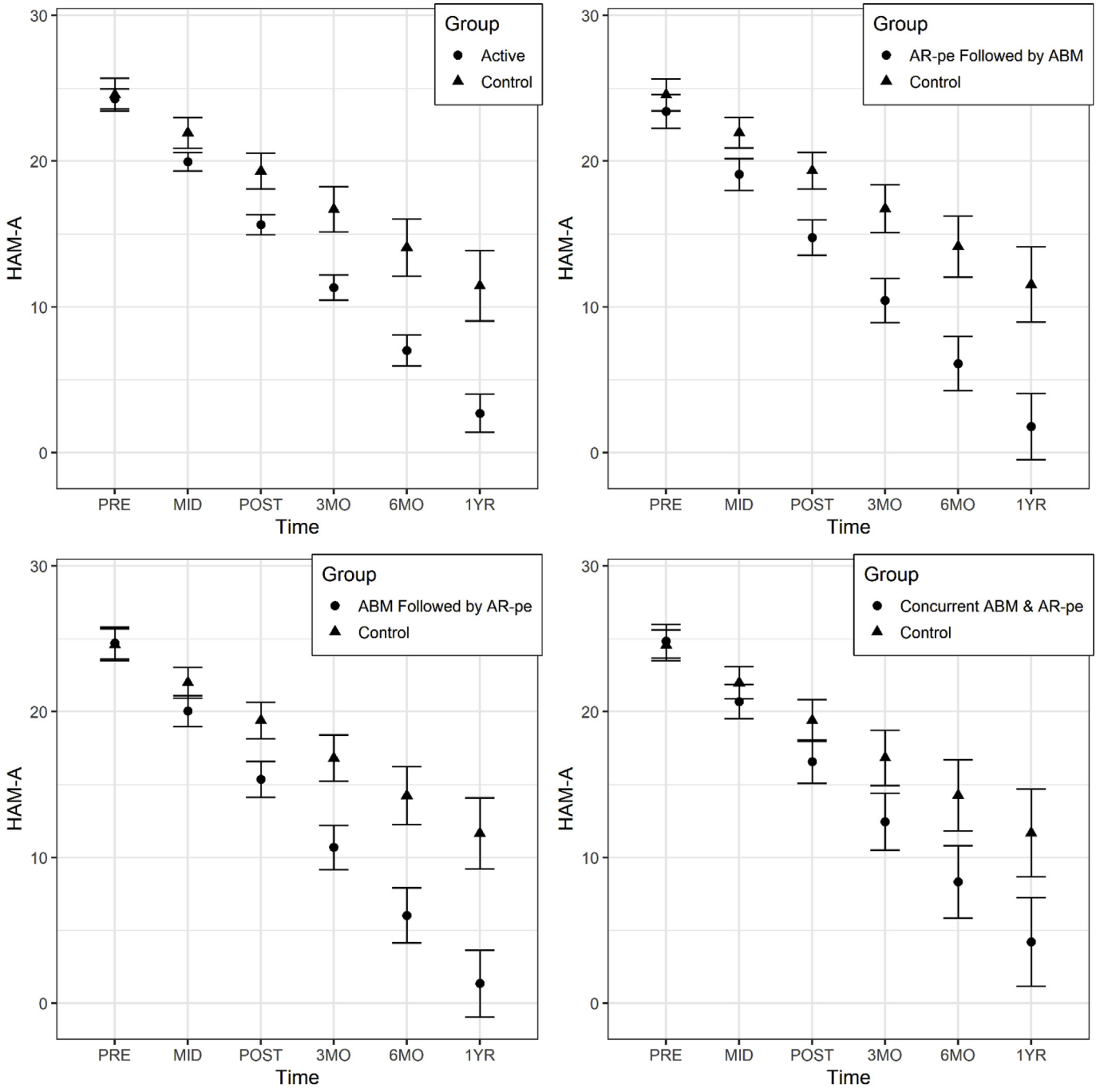

Fig. 2. Graphical representation of linear mixed effects of clinician anxiety rating over time by condition.

$p = .028$, $d = 0.24$). The AR-pe group ($b = 0.71$, $SE = 0.57$, $df = 161$, $t = 1.24$, $p = .215$) and the simultaneous group ($b = 0.68$, $SE = 0.57$, $df = 140$, $t = 1.20$, $p = .231$, $d = 0.18$) did not show any Time-by-Condition interactions.

When examining our secondary outcome measure, the PSWQ, we found a significant interaction of Time-by-Condition ($b = -1.92$, $SE = 0.77$, $df = 338$, $t = -2.49$, $p = .013$, $d = 0.31$). However, contrary to our hypothesis, the control group showed a larger decrease in worry than did the active groups combined. Follow-up analyses revealed that the control group outperformed the ABM group ($b = -2.27$, $SE = 0.96$, $df = 163$, $t = -2.37$, $p = .019$, $d = 0.32$). There was also a marginally significant interaction for Time-by-Condition when comparing the control group to the AR-pe group on ($b = -1.87$, $SE = 0.97$, $df = 172$, $t = -1.93$, $p = .056$, $d = 0.24$). The analysis comparing the simultaneous group to controls did not show any Time-by-Condition interaction ($b = -1.63$, $SE = 1.07$, $df = 151$, $t = -1.52$, $p = .132$, $d = 0.24$). Other self-report measures (BDI and STAI-S) show similar patterns to the PSWQ, but there were no significant Time-by-Condition interactions for active versus control comparison or individual group versus control comparisons[3]

4. Discussion

In the current study we examined the feasibility and effectiveness of

[3] See supplemental materials for detailed Tables & Figures on secondary outcomes.

a home-based self-administered computerized treatment using ABM and AR-pe in individuals diagnosed with GAD. We assigned participants meeting a primary diagnosis of GAD to sequenced or simultaneous ABM and AR-pe groups and compared them to a clinical monitoring control group. The active training groups (sequenced ABM and AR-pe, and simultaneous ABM and AR-pe) showed significant symptom severity reductions over time on our primary outcome measure of anxiety when compared to the control group. Moreover, 41% of patients who received any treatment no longer met diagnostic criteria on our primary measures of anxiety at post-assessment and were considered remitted. In contrast, only participants who received sequenced ABM group showed significant improvement in functional disability. However, these results were not corroborated on self-report measure of worry. Contrary to our hypothesis, the control group outperformed the active groups on this self-report measure. This is consistent with previous studies that found discrepancies between improvement in HAM-A and PSWQ for participants receiving AR, as well as participants receiving non-directive therapy (e.g., Borkovec & Costello, 1993).

Both AR-pe and ABM's are less cognitively demanding than the need to learn cognitive strategies instead relying on implicit learning (Bar-Haim, 2010). Thus, these findings suggest that ABM and AR-pe may be a readily deliverable, effective, and accessible treatment option for individuals with GAD for anxiety.

Our results replicate and extend a growing literature examining the effectiveness of at-home interventions that may help reduce the service implementation gap (Gunter & Whittal, 2010; Wang et al., 2005), and encourage the development of services that are readily deliverable. Moreover, using a clinical sample to determine effectiveness, we were able to generalize our treatment to a relatively clinically intractable condition such as GAD. The current study attempted to address both effectiveness and efficacy in a single sample. Using an active control group in our randomized controlled trial design allowed us to examine the specific and non-specific effects of the interventions. In our sample 19% of those assigned to the control condition met remission criteria for GAD. At first glance this rate of remission may seem high for clinically diagnosed group of individuals with GAD. Indeed, compared to both psychological (22% of weighted response; Smits & Hofmann, 2009) and pharmacological (reviews show 40–60%; Baldwin, Waldman, & Allgulander, 2011) treatments for GAD, these rates are below the typical response rate for studies that have offered a credible control group.

We also examined the effect of sequenced and simultaneous presentation of our two active interventions (ABM and AR-pe) on our outcomes. Recent trials comparing monotherapies (e.g., CBT, pharmacology) with combination therapies demonstrate equivalent or better effects for monotherapies compared to combination therapies (Barlow, Gorman, Shear, & Woods, 2000; Foa et al., 2005). Results from the current study also demonstrate small-to-medium effects for both sequenced and combination therapies. However, in contrast to previous examinations that found combination therapy groups outperform control conditions (Barlow et al., 2000; Foa et al., 2005), our results show that while the sequenced therapies outperformed the control group in rate of improvement for clinical outcomes, our simultaneous group did not.

Our preliminary compliance examination revealed that individuals assigned to simultaneous ABM and AR-pe treatment completed fewer AR-pe and ABM tasks compared to those in the sequenced conditions even though the instructions were such that the latter condition should have completed twice as many sessions. Our results suggest that despite allowing more time and instruction to complete additional at-home therapy, non-usage attrition rates indicated that participants are less inclined to do so. Participant improvement over time may have suffered due to increased task demands and expectations for improvement. Consequently, for both practical and theoretical reasons, sequenced therapies for at-home interventions may be better suited as a first line intervention for GAD.

Our study has additional limitations. First, ABM has historically demonstrated mixed results and some have characterized ABM RCTs as sub-optimal (Cristea et al., 2015). However, meta-analyses have demonstrated reliable dose effects for ABM in reducing symptoms of anxiety in clinical samples (Price et al., 2016). Our study addressed some of these issues including, larger sample size and examining efficacy outside the lab. However, issues remain; for example, our choice of design that precludes addressing questions regarding the independent effect of ABM.

Indeed, in an earlier version of the study, we contemplated using pure groups only. However, based on comments from reviewers and feedback from NIMH program officers, the final revisions of the design included the examination of the crossover effect of the treatments. Although this change reflected an improvement in terms of providing all participants with an active ingredient, it did preclude asking important research questions regarding the specificity of each intervention. Finally, in our attempt to make the ABM task more relevant to participants we used an idiographic material selection procedure. However, by its nature, this design feature did not allow us to control fully for word features (e.g., matching number of letters and frequency of usage in the English language when comparing threat and neutral words).

Data collected at-home may not be an accurate representation of consistent use due to lack of control outside a laboratory setting. One effect of this lack of control was our lack of ability to accurately estimate at home usage of the program. Dropout rates in longitudinal studies range from 7.2% to 44.2% in recent reviews (Davies, Morriss, & Glazebrook, 2014). One reason for this wide range of dropout may be the various definitions used in different studies when the intervention is delivered outside of the laboratory. Our dropout rate of 35.5% (defined as participants who did not return for 6-week assessments after the initial interview and group assignment) was well within the range reported above. Furthermore, our non-usage for ABM and AR-pe was 28.5% and 43.1% respectively for all active groups, and combined delivery did not outperform our control group, possibly due to task demands. As such, the generalizability of the findings is limited to those who are compliant with the at-home program and tasks, and efforts to decrease dropout should be put in place. For instance, future studies should address and attempt to reduce dropout rates by giving both brief technical and clinical support throughout the use of the program (Marks & Cavanagh, 2009). Nonetheless, the findings of the study reflect the use of at-home programs for anxiety in an ecologically valid manner, and therefore is representative of how people use technologies in a familiar, uncontrolled environment. Although we attempted to follow up the participants up to year later, longer follow-up may have provided a better picture regarding the trajectory of GAD given its chronic nature.

Furthermore, in this study as in other randomized clinical trials, a true double-blind is difficult to achieve completely. For example, an active medication may have some side effect that the placebo medication does not have thus unblinding patients or assessors. Similarly, in a CBT trial, clients may mention a component of treatment that may reveal the condition to the assessor. Indeed, multiple studies have documented that patients, study clinicians, and study evaluators can correctly guess patients' treatments at high rates, even under double-blind conditions (Carroll, Rounsaville, & Nich, 1994; Margraf et al., 1991). While our procedures allowed examiners to assess the effect of an intervention relatively unbiased, by no means do these procedures preclude participants or assessors from gaining knowledge about their condition.

The above limitations notwithstanding, we were able to demonstrate the initial efficacy of a low cost, easily accessible treatment for a chronic condition with relatively low response rate in traditional therapies. Home-based computer-delivered treatments including either ABM, AR-pe, or both may be viable treatment options for individuals with GAD who have limited access to resources or are otherwise

unwilling to seek available treatments that require engagement outside of the home.

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Conflict of interest disclosure

Amir was formerly a part owner of Cognitive Retraining Technologies, LLC ("CRT"), a company that marketed anxiety relief products. Dr. Amir's ownership interest in CRT was extinguished on January 29, 2016, when CRT was acquired by another entity. Dr. Amir has an interest in royalty income generated by the marketing of anxiety relief products by this entity.

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Role of funder/sponsor

The agency funding for this study had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Non-author contributions

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Access to data and data analysis

Dr. Amir had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analyses.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brat.2019.103446.

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