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RESEARCH ARTICLE

Attention bias modification add-on to inpatient treatment for young women with anorexia nervosa—A randomized controlled trial

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Abstract

Patients with anorexia nervosa (AN) display elevated anxiety and attention biases (ABs) in threat processing. Attention bias modification treatment (ABMT) is considered promising for anxiety disorders, but its potential for AN is limited. In this study, 154 young women hospitalised because of AN were assigned to ED-related and anxiety-related threat stimuli, or to a non-ABMT intervention control condition in a randomized control trial. Hundred-and-ten patients completed the study. ABMT was an add-on to the regular inpatient treatment. Research participants completed two pretreatment training sessions and eight biweekly sessions of ABMT. AB, ED-related symptoms, depression, anxiety and stress were assessed before and after ABMT in the research groups, and, similarly, 5 weeks apart, in the controls. We found that despite the different patterns of change in AB between the three groups following ABMT, the reduction in AB, or the between-group differences in AB-reduction, were not significant. While the severity of ED-symptoms, depression, anxiety and stress was reduced following ABMT, or control condition, in all groups, there were no between-group differences in these changes. Changes in AB were not correlated with baseline and pre-post-treatment changes in ED-related and comorbid symptomatology. Methodological and inpatient treatment-related considerations may explain our negative ABMT-related results.

KEYWORDS
anorexia nervosa, anxiety, attention bias, attention bias modification treatment, eating disorders

Abbreviations: AB, attention bias; ABMT, attention bias modification treatment; AN, anorexia nervosa; AN-B/P, anorexia nervosa binge/purge type; AN-R, anorexia nervosa restricting type; BMI, body mass index; DASS, Depression Anxiety Stress Scale; ED, eating disorder; EDE-Q, Eating Disorder Examination Questionnaire.

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Highlights

- In the present study, using Attention Bias Modification Treatment (ABMT) did not lead to a reduction in attention bias (AB), while a reduction was found in eating disorder (ED)-related pathology, depression, anxiety, and stress.
- The changes in ED-related pathology, depression, anxiety, and stress following ABMT were not correlated with changes in AB
- The lack of change in AB following ABMT may reflect several methodological considerations, and casts doubt about the potential of ABMT as an add-on treatment in inpatient settings

1 | INTRODUCTION

1.1 | Anorexia nervosa and anxiety

Anorexia Nervosa (AN) is a severe life-threatening condition often associated with a chronic course and unfavourable prognosis (Treasure et al., 2015). The central role of anxiety in the predisposition and maintenance of AN is well established (Pallister & Waller, 2008). Patients with AN may have premorbid anxious traits, often dating back to childhood (Kaye et al., 2004), and the lifetime prevalence of comorbid anxiety disorders in patients with AN range from 23% to 75% (Swinbourne & Touyz, 2007). Importantly, anxiety-related comorbidity has a negative effect on the outcome of AN and has been associated with poor treatment adherence and high drop-out (Kendall & Sugarman, 1997). Thus, studies focussing on the relations between anxiety and AN may offer important insight for improvement of treatment efficacy.

1.2 | Attention bias

Enhanced and prioritised processing of potential threats and rapid response to threat cues facilitate survival. Attention is a key process in such a prioritisation (Shechner et al., 2011). Threat-related attention bias is a pattern of information processing allocating attentional resources to threat over neutral or other competing cues (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007). Automatic allocation of attentional resources to threat-related stimuli might enhance and maintain the individual's anxious state (Mathews & MacLeod, 2002), whereas avoidance of minor threats might serve to regulate anxiety (Bar-Haim et al., 2007).

Threat-related attention bias (AB) is typical in anxious individuals, likely playing a role in predisposing and maintaining their anxiety (Bar-Haim et al., 2007). The specific nature of the anxiety disorder may influence information-processing priorities, with increased sensitivity for disorder-specific threat contents over more general threat contents (Pergamin-Hight, Naim, Bakermans-Kranenburg, van IJzendoorn, & Bar-Haim, 2015).

1.3 | Attention Bias in AN

Studies measuring attentional processes in patients with AN sow elevated AB towards body shape, weight, and food stimuli in comparison to healthy controls (Aspen et al., 2013; Blechert et al., 2010; Brooks et al., 2011; Cardi et al., 2012; Dobson & Dozois, 2004; Giel et al., 2011; Jones-Chesters et al., 1998; Rieger et al., 1998; Shafran et al., 2007; Smeets, Roefs, van Furth, & Jansen, 2008). Considering the high prevalence of social anxiety and generalised anxiety in patients with AN (Cassin & von Ranson, 2005), a few studies have also assessed AB towards social anxiety and general anxiety threat-related stimuli in these patients. Indeed, AB towards anxiety-related words over neutral words (Jones-Chesters et al., 1998), and towards rejecting faces over neutral or compassionate facial expressions (Cardi et al., 2012) has been found in patients with AN compared to controls. In a previous study of our group (Gilon-Mann et al., 2018), patients with restricting type AN (AN-R) have shown vigilance to both ED-related and social anxiety and general anxiety related threat words, whereas patients with binge-purge type AN (AN-B/P) have shown avoidance of both threat types.

1.4 | Attention Bias Modification Treatment

Attention bias modification treatment (ABMT) may provide a promising approach in the treatment of anxiety. Given that biased attention maintains anxiety, ABMT is designed to reduce the orientation of patients towards anxiety-related stimuli (Renwick et al., 2013). In ABMT, AB is targeted directly but implicitly, during computer-based training trials, mostly of a dot-probe task. In each

trial of the dot-probe task, a pair of threat and neutral stimuli appear simultaneously, followed immediately by a probe. The probe appears more frequently in the neutral stimuli location, creating congruency between neutral stimuli and probe location, thus encouraging a decrease in attention allocation to threat (Bar-Haim et al., 2010).

ABMT was investigated in studies of nonclinical, subclinical and clinical participants, mostly diagnosed with anxiety, usually showing small-to-medium effect sizes in reducing anxiety symptoms (Fodor, et al., 2020; Gober et al., 2021; Jones & Sharpe, 2017; Lazarov & Bar-Haim, 2021; Linetzky et al., 2015; Price et al., 2016).

1.5 | ABMT in eating disorders

Currently, there are only preliminary findings about the effectiveness of ABMT in disordered eating. Turton et al. (2016) suggest that ABMT may lead to medium effect sizes in reducing attentional avoidance of food stimuli and, in turn, unhealthy food intake, in adults with non-clinical eating disorders (EDs). Similarly, Fodor et al. (2017) and Kakoschke et al. (2014) propose that ABMT may be a promising intervention for obesity, binge eating disorder (BED) and adults considered addicted to food.

To our knowledge, no clinical randomized control trails (RCTs) examining ABMT with food stimuli have been conducted in patients with EDs. Nonetheless, Renwick et al. (2013) note that a range of threat stimuli might be suitable in ABMT in ED patients, including stimuli related to food, body, social anxiety, social appearance anxiety, perfectionism, and self-criticism. Indeed, ABMT geared towards reducing vigilance to pictures of negative face expression has been found effective in a pilot study of adult inpatients with AN (Cardi et al., 2015). Along the same lines, a review of the efficacy of ABMT for appearance-related stimuli among healthy, subclinical and clinical populations suggests large effects of ABMT on attention, however with no reduction in ED symptoms (Matheson et al., 2019).

1.6 | Aims and hypotheses

The aim of the present study was to examine in an RCT the use of an adjusted version of ABMT involving training with ED-related threat stimuli compared to social and general anxiety-related threat stimuli in adolescent and young adult females hospitalised because of AN. The following were our hypotheses: (1) ABMT would reduce AB towards both ED-related and anxiety-related threat stimuli; (2) The use of ABMT would lead to greater reduction of self-reported ED symptoms in patients in an ED-related threat-stimuli-group relative to an anxiety-related threat-stimuli-group and a control group; (3) Similarly, ABMT would lead to greater reduction in self-reported anxiety symptoms in patients in an anxiety-related threat-stimuli-group relative to the other two groups; (4) Baseline AB would be correlated with parameters related to the severity AN and comorbid psychiatric symptomatology (5) Changes in AB from baseline to post-treatment would be correlated with changes from baseline to post-treatment in ED and comorbid symptomatology. In addition, to rule out the potential confounder effect of AN-subtype, we assessed whether the belonging of the patients to either the AN-R or the AN-B/P subtype would affect our results; this relates to the greater impulsivity and impaired inhibitory control shown in AN-B/P (Wu et al., 2013), the greater cognitive rumination and attention to detail in AN-R (Roberts et al., 2013), and the findings of our previous study (Gilon-Mann et al., 2018), showing vigilance of attention towards anxiety-related stimuli in AN-R but avoidance of these stimuli in AN-B/P.

2 | METHODS

2.1 | Participants

The study included 154 female patients with AN, hospitalised in either the adolescent or the adult ED inpatient departments at the Sheba Medical Center, Tel Hashomer, Israel. Inclusion criteria were: (1) female gender; (2) age between 12 and 25 years; (3) a good understanding of the Hebrew language. Exclusion criteria were lifetime or current schizophrenic spectrum disorders, bipolar disorders, substance use disorders, organic brain disorders, intellectual disability, and any medical illness or chronic mediation use potentially affecting appetite or weight (e.g., diabetes mellitus, thyroid disorders, or chronic use of steroids). The sample included all female patients hospitalised in the two departments between 01/01/15 and 01/10/20, fulfiling these inclusion and exclusion criteria and agreeing to participate in the study (parental consent was required for minors under the age of 18). Forty-four participants (28.57%) dropped-out from the study either because of being released from the hospital before undergoing all the ABMT trials ($n = 25$), or because of wising to end the study prematurely ($n = 19$). The final sample included 110 patients.

The study was approved by the Helsinki Institutional Committee of the Sheba Medical Center (SMC-14-179, 14/12/14) and by the Research Ethics Committee of the Academic College of Tel Aviv– Yaffo (Nr#. 1794-14-SMC,

2020, nr#. 41440 for adult participants, nr#. 41441 for adolescent participants). All patients and their parents (in the case of minors under age 18) agreed to participate in the study by signing a written informed consent after receiving an explanation about the aims and procedures of the study.

In accordance with the hospital protocol of integrative treatment, all patients have received their usual multimodal treatment regimen during their participation in the ABMT study. Although there are differences in the treatment provided in the two departments, the protocol treatment of both adult and adolescent inpatient departments includes a behaviourally oriented nutritional rehabilitation program, different types of individual psychotherapy, family therapy or parental consultation, and various group therapies.

2.2 | Instruments

Diagnosis of AN was achieved using a semi-structured interview, based on the diagnostic criteria of AN of the DSM 5 (APA, 2013). Demographic and clinical variables, including age, education level, and duration of illness and of inpatient treatment were recorded using a self-report demographic questionnaire and from the patients' medical records.

The participants responded to the following self-report questionnaires:

2.2.1 | Eating disorder examination questionnaire (EDE-Q)

The *Eating Disorders Examination-Questionnaire* version 6.0 (EDE-Q; Fairburn & Beglin, 1994) is a 36-item scale assessing restricting and binge-purge pathologies. Higher scores indicate greater pathology. The EDE-Q has been translated to Hebrew and validated in previous studies in Israel (Gilon-Mann et al., 2018; Zohar et al., 2017). The internal consistency of the EDE-Q in the present study was $\alpha = 0.741$ for the Restriction subscale, $\alpha = 0.754$ for the Eating Concern subscale, $\alpha = 0.815$ for the Weight Concern subscale, $\alpha = 0.956$ for the Shape Concern subscale and $\alpha = 0.930$ for the total EDE-Q score.

2.2.2 | Depression Anxiety Stress Scale (DASS-21)

The DASS (Lovibond & Lovibond, 1995) is a 21-item scale assessing depression, anxiety, and stress. Higher scores indicate greater pathology. The DASS has been previously used in patients with EDs (Cardi et al., 2015; Stefanini et al., 2019), including in Israeli populations (Gilon-Mann et al., 2018). The Hebrew translation of the DASS has been validated in previous studies (Halpern et al., 2014). The internal consistency of the DASS in the present study was $\alpha = 0.887$ for the Depression subscale, $\alpha = 0.832$ for the Anxiety subscale, and $\alpha = 0.887$ for the Stress subscale.

2.2.3 | Attention bias assessment: The dot-probe task

Threat-related attention bias has been evaluated using a Hebrew adapted version (see Gilon-Mann et al. (2018) for the ED-related adapted Hebrew version) of the classic word-based dot-probe task (MacLeod et al., 1986; Rieger et al., 1998). Figure 1 presents the sequence of events in a dot-probe task trial. The task consists of 160 trials in which threat–neutral word pairs are presented in a randomized order. Each trial begins with a central fixation '+' (500 ms.), followed by a vertically aligned word pair written in 1-cm-high white block text (500 ms.). One word appears directly above, while the other appears directly below the location vacated by the preceding fixation signal. The two words are separated by 3-cm distance. The pair of words is then replaced by a target probe appearing in either the threat word (congruent trial) or the neutral word (incongruent trial). Probe type is being determined randomly on each trial and is either the letter 'E' or 'F'. Participants are required to identify which of the two probe types appears by pressing the corresponding key as quickly as possible without compromising accuracy. The participant's response clears the screen, and the next trial begins 500 ms later. Response latencies to the probe provide a 'snapshot' of attention, with faster responses to probes occurring at the attended location, relative to the unattended location. The probe is presented with equal probability in the location of the neutral and threat stimuli. Threat bias is calculated by subtracting the mean response time for threat-location probes from the mean response for neutral-location probes. Hence, positive bias scores represent attention bias towards threat, that is, approach, and negative bias scores represent bias away from threat, that is, avoidance (Bar-Haim et al., 2007; Gilon-Mann et al., 2018). Word valance location, target location and target type are fully counterbalanced.

The word stimuli in the present study consisted of one of two sets of 32 threat–neutral word pairs: ED-related threats (e.g., 'FAT') or general and social anxiety related threats (e.g., 'DEAD' or 'GUILT'). The General/social set included an equal proportion of social and general anxiety-

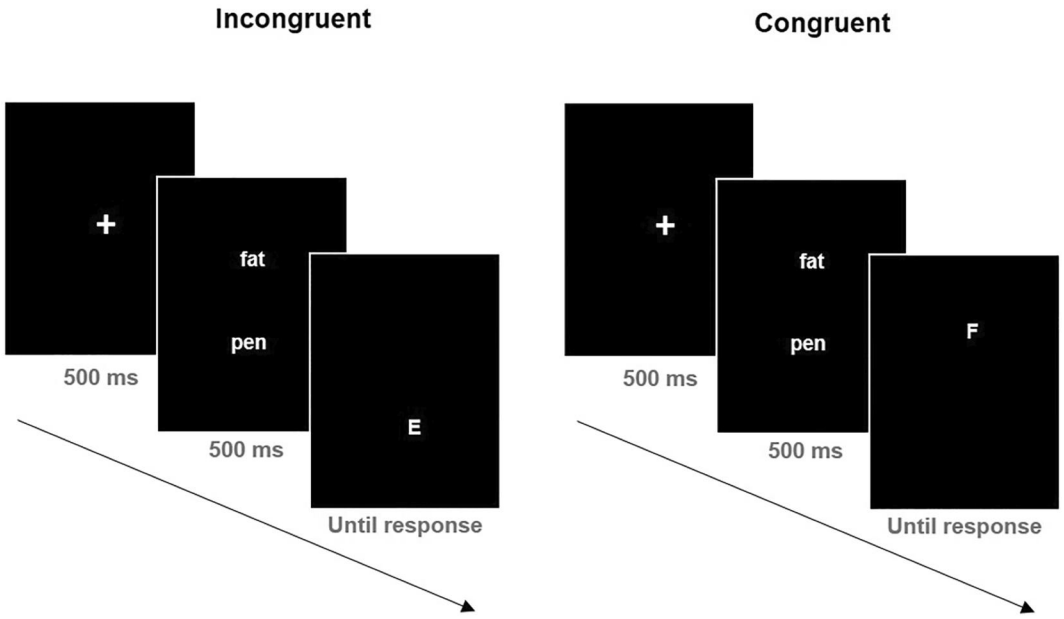

FIGURE 1 Sequence of events in a dot-probe trial. Left panels represent a threat-incongruent trial; right panels represent a threat-congruent trial

related words. Within each pair, word length and frequency of use in Hebrew were matched. The general and social threat words were taken from Bar-Haim et al. (2010) assessing the use of ABMT in different types of anxiety. The ED-related threat words were used in our previous study of attention bias in AN (Gilon-Mann et al., 2018). They were first rated for emotional valence by 15 independent judges working in the adult and adolescent ED departments of the Sheba Medical Center (clinical psychologists, clinical social workers, psychiatrists and dieticians - all not part of the research team). The ratings were used to select words pairs for which the ED-related threat word was rated as negative and its neutral counterpart was rated as neutral. Every word pair was presented five times in the task, resulting in 160 trials. The dot-probe trials were randomized each time.

The use of the dot probe method in this study relied on the standard parameters conducted by the 'TAU-NIMH ABM Initiative' (http://people.socsci.tau.ac.il/mu/anxietytrauma/research/) from where we took the assignments and the ABMT.

2.2.4 | Attention Bias Modification Treatment

Attention Bias Modification Treatment (ABMT) is a computerised training task, utilising an adjusted version of the AB assessment task. The treatment aims to manipulate threat-related ABs by systematically redirecting attention away from the threat stimuli. Neutral and threat stimuli are presented simultaneously, but the probe appears only at the location of neutral stimuli. This repeated coupling of the neutral stimuli with probe location is intended to induce a gradual change in the attentional processes away from threat stimuli (Bar-Haim, 2010). For participants completing ABMT, all trial response times (RTs) shorter than 150 ms or longer than 2000 ms, all trials in which an incorrect response was made, and all trials in which the response time was 2.5 standard deviations of the participant's mean, have been excluded from subsequent analyses (<2% of all trials).

2.3 | Procedure

Patients were interviewed with a DSM 5 (2013) -based semi-structured interview for the diagnosis of AN by experienced adult or child and adolescent psychiatrists working in the respective ED departments at the Sheba Medical Center, Tel Hashomer, Israel. Diagnoses were confirmed in clinical team meetings of the two departments. Only those patients for whom there was a unanimous agreement about their AN diagnosis could enter the study.

Each patient was randomly assigned to one of the threat stimuli groups (ED-related threat, anxiety-related threat) or to the control group by one researcher (HD). The randomisation was such that for every consecutive triad of patients entering the study, the first received the ED-related stimuli condition, the second the social/general anxiety stimuli condition, and the third the control condition. The control participants received only neutral

stimuli in the same manner that each research group received the respective threat stimuli. All participants were blind to their group allocation. Each patient received a specific code known only to one researcher (HD). The coded list of the patients was kept in a specie file in a computer by the principal investigator (DS) who was the only one with access to this file. The flow-chart of the allocation of the patients throughout the study is described in Figure 2. All participants received during the ABMT the multimodal protocol for the treatment of EDs of the respective department.

The weight and height of the patients were measured weekly during the morning hours, according to standardized procedures (Tanner, 1994). Patients could enter the study within 3 weeks after their admission to inpatient treatment, when their medical condition and treatment regimen were considered stabilised. Patients were not receiving psychotropic medications during the time of the study, except for emergency conditions. Testing for all patients in all sessions was administered individually, in a quiet room during the morning hours, between meals, to reduce the influence of food consumption on the results of the study. The dot-probe task and self-report questionnaires were administered by a single researcher (HD), a M.A. medical psychology student.

Patients carried out the computerised training sessions twice a week. Each session lasted approximately 6 minutes. Altogether, each participant completed 9 be-weekly dot-probe sessions: eight be-weekly training sessions and two assessment trials before the training sessions. Altogether, the study lasted for 5 weeks. The self-rating questionnaires were distributed twice, 5 weeks apart, in the beginning and end of the study, in random order, after the completion of the AB assessment tasks.

2.4 | Statistical analyses

First, we used independent *t*-tests and Chi-square analyses to compare between participants completing and not completing ABMT. Variables that were significantly different between completers and non-completers were statistically controlled in further analyses. We also compared the baseline pre-treatment AB, EDE-Q and DASS-21 parameters of patients with AN-R and AN-B/P, and patients younger and older than 18 (i.e., hospitalised in the adolescent and adult ED department, respectively). In addition, we used one-way analysis of variance (ANOVA) and Sidak post-hoc analyses to compare between the three groups in the baseline demographic clinical, and psychometric characteristics.

We then used an intention-to-treat approach, which includes all participants randomized into the treatment groups at baseline. Thus, we used Mixed Effects Modelling to compare the differences in the AB patterns (response time [RT] and accuracy rates) before and after the ABMT, and between the groups. We also used Mixed Effects Modelling to compare the between-group differences in the self-report questionnaires scores before and after the ABMT in a 3 (stimuli type; ED-related threat, anxiety-related threat, Control group) X 2 (time; pre\post treatment) design. Effect size was calculated for these analyses.

Pearson correlation tests were used to investigate the correlations between AB at baseline and baseline demographic, clinical and psychometric variables, as well as between the changes in AB from baseline to post-treatment and the respective changes in the clinical and psychometric variables introduced. Significance was set at $p < 0.05$. Statistical analysis was carried out using SPSS (Version 25).

3 | RESULTS

3.1 | Demographic, clinical, and psychometric variables

The study included 154 female participants with AN of whom, 110 (71.4%) participants completed the ABMT training and post-treatment assessment. The mean age of this sample was 17.90 years (SD = 3.61) and mean baseline BMI was 16.94 kg/m^2 (SD = 2.20). The differences between participants completing and not completing ABMT are summarised in Table 1. Participants withdrawing from treatment were significantly older, mostly adults, with a longer duration of illness and more previous hospitalizations than participants completing the intervention. The two groups did not differ in BMI, days of hospitalisation until the beginning of ABMT, rate of AN-R diagnosis, and baseline AB, EDE-Q, and DASS-21 scores (see Table 1).

Table 2 summarises the findings for the baseline variables of patients with AN undergoing ABMT. No between-group differences were found for the demographic and clinical items. Comparison of the baseline psychometric variables between the groups (Table 2), showed no between-group differences for AB (both RT and accuracy), and all EDE-Q subscales.

Between-group differences were found for all DASS-21 scales: First, for baseline DASS-21Depression ($F(2,148) = 3.38$, $p = 0.037$), higher depression was reported by the ED-stimuli group in comparison with the control group (post hoc $p = 0.033$). No difference was found between the anxiety-stimuli and control groups (post hoc $p = 0.28$). Second, for baseline DASS-21 Anxiety (F

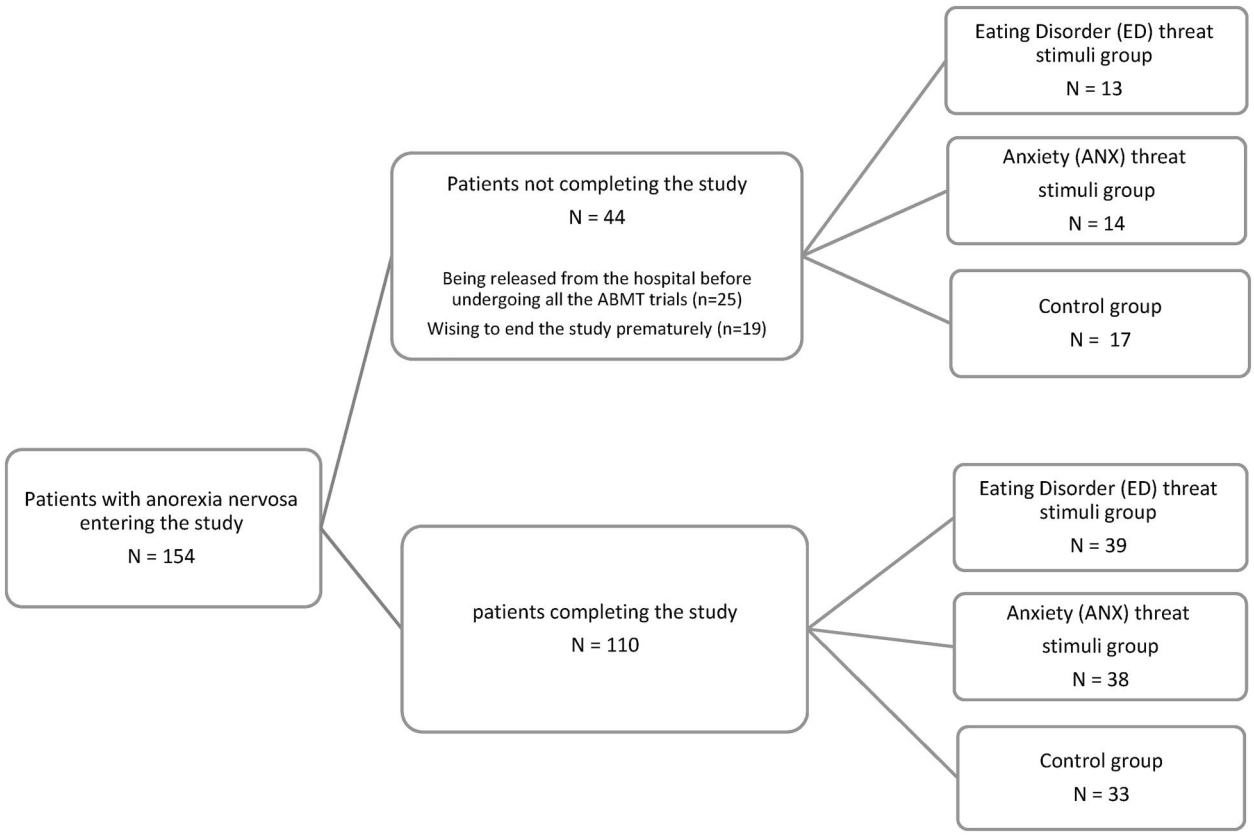

FIGURE 2 Flowchart of the trial

(2,148) = 5.201, $p = 0.007$), higher anxiety was reported by both the ED-stimuli group (post hoc $p = 0.019$) and the anxiety-stimuli group (post hoc $p = 0.015$) in comparison with the control group. Last, for baseline DASS-Stress (F (2,148) = 6.921, $p = 0.001$), higher stress was reported by both the ED-stimuli group (post hoc $p = 0.002$) and the anxiety-stimuli group (post hoc $p = 0.009$) in comparison with the control group.

Table 3 summarises the baseline differences between patients with AN-R and AN-B/P. No differences were found for both AB RT and AB accuracy. Although patients with AN-R showed AB vigilance towards the anxiety provoking stimuli (a positive RT score of 3.62 (23.27) ms.), and patients with AN-B/P showed avoidance of the anxiety provoking stimuli (negative RT score of −0.88 (20.75) ms. see Table 3), these differences were not significant. This allowed us to combine the two AN subtypes with respect to the analysis of ABMT. Patients with AN-B/P showed higher scores on the EDE-Q-Eating Concerns, DASS-21 Anxiety, and DASS-21 Stress (see Table 3). Last, no differences in the baseline psychometric variables (AB, EDE-Q, DASS-21) were found when assessing the patients according to being younger than 18, that is, hospitalised in the adolescent ED department, or older than 18, that is, hospitalised in the adult ED department (results not shown). This allowed us to combine the groups with respect to the analysis of ABMT.

4 | OUTCOME

4.1 | Accuracy measures

The final sample had a mean accuracy rate of 93.51% (SD = 7.41) at baseline and 95.36% (SD = 4.51) at post-treatment. Table 2 summarises the between group differences at baseline, and Table 4 the between-group differences in the change from pre- to post ABMT. No between-group significant difference was found in pre-treatment [F(2.148) = 1.130, $p = 0.326$; see Tale 2]. A Mixed analysis indicated that the time effect for ABMT accuracy was significant (F(1,151) = 7.530, $p = 0.007$; effect size = 0.8), but the time by the ED stimulus interaction (F(1,151) = 0.121, $p = 0.729$; effect Size = 0.02) and the time by the anxiety stimulus interaction (F(1,151) = 1.288, $p = 0.258$; effect Size = 0.03) were not significant (see Table 4).

TABLE 1 Baseline demographic, clinical and psychometric parameters of patients with AN completing/not completing the study

	Completers ($N = 110$)	Non-completers ($N = 44$)	$t(1,152)/\chi^2_{(1)}$	p
Age (years)	17.90 (3.61)	20.41 (3.43)	3.991	$p < 0.001$
Adolescent inpatients, number (%)	$N = 59$ (53.67%)	$N = 7$ (15.91%)	$\chi^2_{(1)} = 18.266$	$p < 0.001$
Years of illness	3.47 (3.43)	6.32 (3.86)	4.448	$p < 0.001$
Baseline BMI (kg/m^2)	16.94 (2.20)	16.79 (2.17)	−0.392	$p = 0.695$
Number of previous hospitalizations	0.77 (1.48)	1.55 (1.69)	$\chi^2_{(1)} = 2.806$	$p = 0.006$
Days of inpatient treatment before ABMT	26.34 (22.76)	24.71 (3.72)	−0.356	$p = 0.722$
AN-R diagnosis, number (%)	$N = 67$ (60.90%)	$N = 20$ (45.45%)	$\chi^2_{(1)} = 3.054$	$p = 0.081$
ED stimuli, number (%)	$N = 39$ (35.45%)	$N = 13$ (29.54%)		
ANX stimuli, number (%)	$N = 38$ (34.54%)	$N = 14$ (31.81%)	$\chi^2_{(2)} = 1.116$	$p = 0.572$
Control stimuli number (%)	$N = 33$ (30%	17 (38.6%)		
Baseline AB RT (ms.)				
ED stimuli	4.75 (20.83)	−0.50 (24.17)	−7.58	$p = 0.452$
ANX stimuli	−1.32 (20.76)	1.66 (33.05)	0.390	$p = 0.698$
Control condition	2.36 (21.35)	2.76 (26.37)	−0.950	$P = 0.90$
Baseline AB accuracy				
ED stimuli	93.17% (6.80)	93.17% (6.86)	−0.295	$p = 0.770$
ANX stimuli	92.25% (10.05)	92.72% (6.21)	0.163	$p = 0.871$
Control condition	92.75% (7.05)	93.10% (7.35)	−0.275	$P = 0.783$
EDE-Q restriction	4.21 (1.82)	4.59 (1.65)	1.137	$p = 0.258$
EDE-Q eating concern	3.33 (1.67)	3.68 (2.57)	0.957	$p = 0.340$
EDE-Q weight concern	4.08 (1.89)	3.36 (2.28)	−1.926	$p = 0.056$
EDE-Q shape concern	4.56 (1.64)	3.93 (1.92)	−1.967	$p = 0.051$
EDE-Q total	4.05 (1.48)	3.89 (1.74)	−0.539	$p = 0.591$
DASS-21 depression	16.41 (9.75)	18.15 (10.08)	0.965	$p = 0.336$
DASS-21 anxiety	11.99 (8.48)	15.10 (11.18)	1.828	$p = 0.070$
DASS-21 stress	15.97 (8.83)	16.70 (9.92)	1.47	$p = 0.143$

Abbreviations: AB, attention bias; ABMT, Attention Bias Modification Treatment; AN, anorexia nervosa; AN-R, anorexia nervosa restricting type; ANX-stimuli, anxiety-related threat stimuli; BMI, body mass index; DASS-21, Depression Anxiety and Stress Scale-21; ED-stimuli, eating disorder-related threat stimuli; EDE-Q, Eating Disorders Examination Questionnaire; ms, milliseconds; RT, response time.

Hypothesis 1 *ABMT will reduce the bias towards the threat stimuli in both stimuli groups*

Participants in the ED-related threat-stimuli-group showed AB towards the threat stimuli at baseline (mean pre-training RT = 3.43 ms., SD = 21.58). Following ABMT, this group showed reduction in AB towards the threat-stimuli (Mean post-training RT = 0.24, SD = 22.01). Participants in the anxiety-related threat-stimuli-group showed attentional avoidance of the threat stimuli at baseline (Mean pre-training RT = −0.52 ms., SD = 24.35). Following ABMT, this group showed a shift in AB towards the threat-stimuli (mean post-training RT = 2.20 ms., SD = 23.34). Participants in the control group showed AB towards the threat stimuli at baseline (mean pre-training RT = 2.09 ms., SD = 20.87). Following ABMT, this group showed no change in AB towards the threat-stimuli (Mean post-training RT = 2.62 ms., SD = 21.46; See Table 4). However, the use of a Mixed Model analysis showed that neither the time effect (F(1,151) = 0.008, $p = 0.923$; Effect Size = 0.01) nor the time by stimuli interaction effect for ED (F(1,151) = 0.505, $p = 0.479$; Effect Size = 0.01) or anxiety (F(1,151) = 0.175, $p = 0.676$; Effect Size = 0.01) related threat stimuli were significant (see Table 4).

In addition, as our sample included both adolescents and young adults (age range 12–25 years), we analysed

TABLE 2 Baseline demographic, clinical and psychometric variables of patients with AN undergoing ABMT

	ED stimuli ($N = 52$)	ANX stimuli ($N = 52$)	CN ($N = 50$)	F(2,148)	p
Age (years)	17.94 (3.16)	18.85 (4.21)	19.07 (3.63)	1.335	$p = 0.266$
Adolescent inpatients, number (%)	$N = 20$ (61.5%)	$N = 21$ (40.4%)	$N = 25$ (50.0%)	$\chi^2_{(2)} = 1.582$	$p = 0.453$
Years of illness	3.81 (2.91)	4.11 (4.09)	4.97 (4.19)	1.286	$p = 0.279$
Baseline BMI (kg/m^2)	16.73 (1.97)	16.99 (2.56)	16.98 (2.01)	0.236	$p = 0.790$
Number of previous hospitalizations	0.85 (1.17)	1.23 (2.05)	0.90 (1.35)	0.901	$p = 0.408$
Hospitalisation days until the beginning of ABMT	26.55 (22.41)	25.76 (27.83)	25.40 (18.90)	0.032	$p = 0.968$
AN-R diagnosis, number (%)	$N = 30$ (57.7%)	$N = 27$ (51.9%)	$N = 30$ (60.0%)	$\chi^2_{(2)} = 0.722$	$p = 0.697$
Baseline AB RT (ms.)	3.43 (21.58)	−0.52 (24.35)	2.09 (20.87)	0.421	$p = 0.657$
Baseline AB accuracy	93.6% (6.56)	92.3% (9.12)	94.5% (6.12)	1.130	$p = 0.326$
EDE-Q restriction	4.48 (1.72)	4.59 (1.58)	4.64 (1.55)	0.131	$p = 0.878$
EDE-Q eating concern	3.82 (1.46)	4.00 (1.31)	3.59 (1.45)	1.091	$p = 0.339$
EDE-Q weight concern	4.75 (1.56)	4.96 (1.46)	4.84 (1.42)	0.249	$p = 0.780$
EDE-Q shape concern	4.90 (1.35)	5.15 (1.17)	4.98 (1.34)	0.506	$p = 0.604$
EDE-Q total	4.49 (1.32)	4.68 (1.23)	4.51 (1.29)	0.322	$p = 0.725$
DASS-21 depression	19.08 (12.01)	17.27 (10.28)	14.08 (5.15)	3.380	$p = 0.037$
DASS-21 anxiety	14.38 (10.01)	14.55 (10.52)	9.33 (5.89)	5.201	$p = 0.007$
DASS-21 stress	19.02 (10.78)	18.29 (11.26)	12.48 (5.14)	6.921	$p = 0.001$

Abbreviations: AB, attention bias; ABMT, Attention Bias Modification Treatment; AN, anorexia nervosa; AN-R, anorexia nervosa restricting type; ANX-stimuli, anxiety-related threat stimuli; BMI, body mass index; DASS-21, Depression Anxiety and Stress Scale-21; ED-stimuli, eating disorder-related threat stimuli; EDE-Q, Eating Disorders Examination Questionnaire; ms., milliseconds; RT, response time.

TABLE 3 Baseline comparison of patients with AN-R and AN-B/P

	AN-R ($N = 87$)	AN-B/P ($N = 67$)	t	p
Baseline AB RT (ms.)	3.62 (23.27)	−0.88 (20.75)	1.24	$p = 0.214$
Baseline AB accuracy	92.2% (8.3)	94.1% (5.2)	1.33	$p = 0.186$
EDE-Q restriction	4.42 (1.69)	4.77 (1.50)	1.32	$p = 0.188$
EDE-Q eating concern	3.54 (1.44)	4.15 (1.30)	2.71	$p = 0.008$
EDE-Q weight concern	4.75 (1.48)	4.98 (1.46)	0.972	$p = 0.333$
EDE-Q shape concern	4.94 (1.26)	5.10 (1.32)	0.740	$p = 0.460$
EDE-Q total	4.41 (1.31)	4.75 (1.22)	1.623	$p = 0.107$
DASS-21 depression	15.94 (9.79)	18.09 (9.84)	1.335	$p = 0.184$
DASS-21 anxiety	11.36 (9.51)	14.73 (8.87)	2.218	$p = 0.028$
DASS-21 stress	15.28 (9.73)	18.52 (9.94)	2.005	$p = 0.047$

Abbreviations: AN-R, anorexia nervosa restricting type; AN-B/P, anorexia nervosa binge/purge type; DASS-21, Depression Anxiety and Stress Scale-21; EDE-Q, Eating Disorders Examination Questionnaire; ms., milliseconds; RT, response time.

AB with a dichotomic age variable (above and below 18 years old). Neither age or age by stimuli interaction had a significant influence on the change in AB RT (results not shown). Similarly, age was not correlated with the change in AB RT and accuracy from pre-to post-ABMT.

TABLE 4 EDE-Q, DASS-21, AB at baseline and post-ABMT, BMI at admission and discharge

	ED stimuli ($N = 52$)	ANX stimuli ($N = 52$)	CN ($N = 50$)	Mixed model time effect F, p	Mixed model time * ED stimuli interaction effect F, p	Mixed model time * ANX stimuli interaction effect F, p
EDE-Q restriction						
Baseline	4.48 (1.72)	4.59 (1.58)	4.64 (1.55)			
Post-treatment	3.01 (2.15)	3.18 (2.13)	3.17 (1.87)	37.97, $p < 0.001$ Effect Size = 0.34	0.001, $p = 0.982$ Effect Size = 0.03	0.103, $p = 0.748$ Effect Size = 0.04
EDE-Q eating concern						
Baseline	3.82 (1.46)	4.00 (1.31)	3.59 (1.45)			
Post-treatment	2.78 (1.67)	2.86 (1.70)	2.70 (1.42)	41.44, $p < 0.001$ Effect Size = 0.34	0.030, $p = 0.863$ Effect Size = 0.01	0.239, $p = 0.626$ Effect Size = 0.02
EDE-Q weight concern						
Baseline	4.75 (1.56)	4.96 (1.46)	4.84 (1.42)			
Post-treatment	4.62 (1.63)	4.44 (1.86)	4.77 (1.55)	2.057, $p = 0.154$ Effect Size = 0.02	0.002, $p = 0.969$ Effect Size = 0.01	1.390, $p = 0.241$, effect Size = 0.01
EDE-Q shape concern						
Baseline	4.90 (1.35)	5.15 (1.17)	4.98 (1.34)			
Post-treatment	4.42 (2.71)	4.09 (2.02)	4.35 (1.80)	9.708, $p = 0.002$ Effect Size = 0.11	0.147, $p = 0.702$ Effect Size = 0.01	0.645, $p = 0.424$ Effect Size = 0.01
EDE-Q total						
Baseline	4.49 (1.32)	4.68 (1.23)	4.51 (1.29)			
Post-treatment	3.71 (1.79)	3.64 (1.80)	3.74 (1.50)	26.835, $p < 0.001$ Effect Size = 0.26	0.024, $p = 0.877$ Effect Size = 0.05	0.313, $p = 0.577$ Effect Size = 0.01
DASS-21 depression						
Baseline	19.08 (12.01)	17.27 (10.28)	14.08 (5.15)			
Post-treatment	13.45 (7.47)	12.92 (7.25)	13.19 (6.83)	42.998, $p < 0.001$ Effect Size = 0.26	10.228, $p = 0.002$ Effect Size = 0.08	5.237, $p = 0.023$ Effect Size = 0.09
DASS-21 anxiety						
Baseline	14.38 (10.01)	14.55 (10.52)	9.33 (5.89)			
Post-treatment	8.78 (6.28)	8.94 (6.64)	6.93 (5.38)	40.955, $p < 0.001$ Effect Size = 0.25	8.478, $p = 0.004$ Effect Size = 0.01	5.678, $p = 0.018$ Effect Size = 0.04

TABLE 4 (Continued)

	ED stimuli ($N = 52$)	ANX stimuli ($N = 52$)	CN ($N = 50$)	Mixed model time effect F, p	Mixed model time * ED stimuli interaction effect F, p	Mixed model time * ANX stimuli interaction effect F, p
DASS-21 stress						
Baseline	19.02 (10.78)	18.29 (11.26)	12.48 (5.14)			
Post-treatment	14.01 (7.84)	14.35 (7.49)	12.67 (5.47)	34.363, $p < 0.001$ Effect Size = 0.22	10.754, $p = 0.001$ Effect Size = 0.12	6.574, $p = 0.011$ Effect Size = 0.10
AB accuracy						
Baseline	93.6% (6.56)	92.3% (9.12)	94.5% (6.12)			
Post-treatment	94.5% (5.43)	95.5% (4.67)	96.1% (3.02)	7.530, $p = 0.007$ Effect Size = 0.08	0.121, $p = 0.729$ Effect Size = 0.02	1.288, $p = 0.258$ Effect Size = 0.03
AB RT (ms.)						
Baseline	3.43 (21.58)	−0.52 (24.35)	2.09 20.87)			
Post-treatment	0.24 (22.01)	2.20 (23.34)	2.62 (21.46)	0.008, $p = 0.928$ Effect Size = 0.01	0.505, $p = 0.479$ Effect Size = 0.01	0.175, $p = 0.676$ Effect Size = 0.01
BMI						
Admi-ssion	16.73 (1.97)	16.99 (2.56)	16.98 (2.01)			
Discharge	19.13 (1.74)	19.23 (2.49)	20.44 (2.21)	28.22, $p < 0.001$ Effect Size = 0.08	12.33, $p = 0.002$ Effect Size = 0.07	13.35, $p = 0.005$ Effect Size = 0.08

Abbreviations: AB, attention bias; ABMT, Attention Bias Modification Treatment; ANX-stimuli, anxiety-related threat stimuli; BMI, body mass index; DASS-21, Depression Anxiety and Stress Scale-21; ED-stimuli, eating disorder-related threat stimuli; EDE-Q, Eating Disorders Examination Questionnaire; ms., milliseconds; RT, response time.

Hypothesis 2 *ABMT would produce greater reduction of ED symptoms on the EDE-Q in the ED-related threat-stimuli-group relative to the other two groups*

Table 4 summarises the findings for this hypothesis. A Mixed Model procedure assessing the severity of ED pathology on the EDE-Q showed that ABMT did not produce a greater reduction of EDE-Q scores at post-treatment in the ED-related threat-stimuli-group compared to the other two groups. In most of the EDE-Q subs-scales, the time main effect was significant but the time by threat-related stimuli interaction effects were not.

Hypothesis 3 *ABMT would produce greater reduction in the DASS-21 subscales in the anxiety-related threat stimuli group relative to the other two groups*

Table 4 summarises the findings for this hypothesis. A Mixed Model procedure assessing the levels of depression, anxiety and stress on the DASS-21 indicated that for all three scales, the time main effect and the time by threat stimuli group interaction effect were significant. The results showed a greater reduction in DSSS-21 Depression in the ED-related and the anxiety-related stimuli groups in comparison with the control group. Moreover, a greater reduction in DASS-21 Anxiety and DASS-21 Stress was found in the ED-related and anxiety-related stimuli groups in comparison with the control group (see Table 4). However, because of the initial between-group differences in all the DASS-21 scales (see Table 2), we conducted a one-way ANOVA for the change from baseline to post-treatment, with the baseline score for each scale as a covariate. The findings for all the scales showed that the stimuli effect was no longer significant: DASS-21 Depression - ($F(2,147) = 0.845$, $p = 0.432$), DAss-21 Anxiety - ($F(2,147) = 1.618$, $p = 0.202$), and DASS-21 Stress - ($F(2,147) = 2.927$, $p = 0.057$). Effect sizes were found to be low to moderate with respect to the size of the sample.

Hypothesis 4 *Changes in AB from baseline to post-treatment would be correlated with baseline clinical and psychometric parameters*

No significant correlations were found between the changes in AB RT from baseline to post-treatment and duration of illness, age before ABMT, type of AN, and baseline EDE-Q ED-related pathology, DASS-21 Depression, DASS-21 Anxiety, DASS-21 stress, and BMI (effect size did not exceed 0.15).

Hypothesis 5 *Changes in AB from baseline to post-treatment would be correlated with the respective changes in the clinical and psychometric parameters*

No significant correlations were found between the changes in AB from baseline to post-treatment and the respective changes in EDE-Q ED-related pathology, DASS-21 Depression, DASS-21 Anxiety, DASS-21 Stress, and BMI (effect size did not exceed 0.15).

Last, BMI significantly improved from admission to the two departments to discharge in all three groups. No significant between-group differences were found in the change in BMI from admission to discharge (see Table 4).

5 | DISCUSSION

The present study sought to replicate and extend the findings of a few previous studies assessing ABMT in AN (Cardi et al., 2015; Renwick et al., 2013), by administering ABMT in an RCT to a large-scale sample of adolescent and young adult women hospitalised because of AN. We hypothesised that ABMT training in a task with either ED-related or general/social anxiety-related threat stimuli would result in a reduction of AB towards the respective threat. We further hypothesised that the assumed reduction of AB towards the respective threat following ABMT would be associated with a parallel reduction in self-reported severity of ED, depression, anxiety and stress-related symptoms. In addition, we hypothesised that changes in AB from pre-to post-treatment would be associated with the baseline demographic, clinical and psychometric parameters introduced in the study and with the change in the psychometric parameters from pre-to post ABMT.

Contrary to our first hypothesis, no significant changes in AB were observed in either type of stimuli group or between the three groups over time. In the ED-related threat-stimuli-group, the trend was towards a reduction in the vigilance to the ED stimuli, approaching almost no bias. In the general/social anxiety-related threat-stimuli-group, there was a transition from a slight avoidance to an AB towards the threat stimuli. No change in AB RT was noted in the control group. Despite the different patterns between the three groups, these differences were not significant. These findings are consistent with studies in anxiety disorders where change in AB was not observed following ABMT (Chau et al., 2019; Ollendick et al., 2019). Similarly, Cristea, Kok, and Cuijpers (2015) suggested that changes in AB in adult patients with anxiety and depression following ABMT were mostly non-significant. Nonetheless, other

studies did find a significant reduction of AB following ABMT in patients with AN (Cardi et al., 2015), anxiety disorders (Amir et al., 2009a, 2009b; De Voogd et al., 2014; Eldar et al., 2012; Pergamin-Hight et al., 2016) and depressive disorders (Dai et al., 2019).

Contrary to our 2nd and 3rd hypotheses, the improvement found in the EDE-Q scales (except for EDE-Q Weight Concern) and the three DASS-21 subscales from pre-to post ABMT were not associated with parallel changes in AB in the ED-related group stimuli, and anxiety-related group stimuli, respectively. MacLeod and Clarke (2015), suggested, in this respect, that ABMT may lead to anxiety reduction only if it successfully reduces the AB to the anxiety-related stimuli threat. Moreover, Cristea, Mogoașe, et al. (2015), conclude that although ABMTs in children and adolescents may lead to moderate effects on targeted biases, their effect on overall mental health is limited.

Unfortunately, despite the random allocation, we found initial between-groups differences in the DASS-21 scores. The control group scored lower than the two threatening-stimuli groups in the baseline measures of all DASS scales. Time by threat stimuli repeated measures ANOVA interactions were significant in all DASS scales, but these findings were no longer significant when controlling for the initial differences as a covariate. Time effect was significant for the EDE-Q and DASS-21 parameters (except for EDE-Q Weight Concern; see Table 4), likely reflecting the influence of the other treatments provided, and of the improvement in the participants' physical condition, on ED-related pathology, depression and anxiety, but not on AB.

Contrary to our 4th and 5th hypotheses, changes in AB from pre- to post-treatment did not correlate with the baseline demographic, clinical and psychometric parameters, or with the change in the psychometric parameters from pre- to post-ABMT. These negative findings are likely accounted by the lack of significant changes in AB over time in all three groups.

The differences between our negative results and the findings of the studies showing a reduction of attention bias post-ABMT may be related to several methodological considerations. First, our control group has received only neutral stimuli in their dot-probe task. The commonly used comparison to ABMT is attention control training (ACT), in which participants complete the same dot-probe task as in ABMT, but in the control condition, the probe appears with equal probability in the locations of the neutral and threatening stimuli in all sessions. ACT allows for the isolation of the added value of ABMT training. Many studies showing notable effects of ABMT, have compared their experimental treatment to a control condition (Amir et al., 2009a, 2009b; Dai et al., 2019; De Voogd et al., 2014; Eldar et al., 2012). Nonetheless, Cardi et al. (2015) have found a significant reduction of AB following ABMT in inpatients with AN in a study design without a control group.

Another distinguishing factor may be related to differences in the tasks used in the ABMT, mostly in the applied stimuli (e.g., words vs. images) and the content of the threatening stimuli. The literature about ABMT in anxiety disorders suggests that utilising words stimuli might lead to bigger effect sizes compared to facial expression pictorial stimuli (Hakamata et al., 2010). A study in EDs also argues that word stimuli are at least as effective as image stimuli for ABMT (Schober et al., 2014). However, Cardi et al. (2015) has found a significant reduction of AB towards rejecting and critical faces in patients with AN using pictorial stimuli. By contrast, the ED-related threat stimuli and the general/social anxiety-related threat stimuli in our study, both presented as words, have not induced a significant reduction in AB. Moreover, the participants' age ranged from 12 to 25, meaning that our sample included both adolescents and young adult females, when children and adolescents might be more sensitive to image stimuli than to words (Dudeney et al. (2015).

Studies usually differ in whether they test ABMT in adolescents or adults. Typically, adolescent samples consist of patients with short duration of illness, whereas adult samples show a longer duration of illness. Adult patients with AN may show greater cognitive rigidity (Treasure et al., 2015), hence greater difficulty to change, potentially leading to a less favourable effect of ABMT. In addition, different ABs to food-related stimuli may exist in adolescents and adults with AN, suggesting that AB may change over time as the illness progresses (Werthmann et al., 2019).

It is of note that we aimed to recruit both adolescent and inpatients with AN, to assess possible differences in the reaction to ABMT over time, using for this purpose one stimuli design for all participants, not taking age into consideration. As noted in the results section, neither age, nor age by stimuli interaction had a significant influence on the effect of ABMT, and changes in AB from pre-to post ABMT did not correlate with age at entering the study. Nonetheless, the lack of use of pictorial stimuli in the younger age groups might have interfered with the lack of influence of age on changes in ABMT.

From a different perspective, regarding the content of the ED-related word stimuli, Levinson et al. (2013) highlighted the relevance of social appearance anxiety, that is, '*the fear that one will be negatively evaluated because of one's appearance*' (Hart et al., 2008) in both EDs and social anxiety. Social appearance anxiety was

not included in the content of the threatening stimuli in our study. Disapproving faces, as included in the study of Cardi et al. (2015) might be more pertinent to social appearance anxiety, likely a more applicable content in patients with AN. In line with this contention, Rowlands et al. (2020) found that social appearance anxiety in the context of exposure to rejection in a virtual environment might trigger ED symptoms.

The fact that our participants were treated in an inpatient setting may also be relevant for the insignificant changes in AB found in our study. First, the participants' mean recruitment time to ABMT was 3 weeks after their admission. During that time, they settled into a stable treatment regime and underwent changes in eating behaviours and weight. The pre-treatment levels of the different tools used might not indicate the levels of pathology on admission.

Second, the participants in our study received other treatments in addition to ABMT. Despite the existence of a similar multimodal approach for the treatment of EDs in both departments, different therapeutic regimens might exist. Nonetheless, it is of note that whereas age (below/above 18) was the one factor differentiating by definition between the two departments, it had no effect on baseline AB or on the change in AB from pre-to post ABMT.

In addition, 28.6% of the participants dropped-out of ABMT because of refusal to continue with the treatment or to complete the post-treatment assessments, or because of being discharged from inpatient treatment before completing the intervention. We did not find differences between completers and non-completers in the baseline measures of EDE-Q, DASS-21, and attentional bias RT/accuracy rates. However, non-completers were older, mostly adults, with longer duration of illness and more previous hospitalizations. The relatively high rate of dropout, alongside the specific characteristics of the non-completers, highlights the difficulty inherent in recruiting patients with long standing AN for treatment studies, even in the case of a seemingly brief and easy intervention.

6 | LIMITATIONS

Our negative results, and the difficulties in interpreting these results, may be explained, at least in part, by the limitations of the study. First, the control participants have received only neutral stimuli and did not undergo a potential control version of ABMT. Second, the other treatments received in the two departments have not been consentient, making it difficult to assess the influence if ABMT as an add-on treatment. Nonetheless our study represents an effort to assign ABMT in a naturalistic rather than a research design. Third, we have sought to study the influence of ABMT in a large group of female patients with AN of different ages, using for that purpose one verbal stimuli-related protocol. Thus, we have not used pictorial threat stimuli that could have been more appropriate for younger participants. Fourth, we have not assessed the influence of psychiatric comorbidities, specifically comorbid anxiety disorders, that could be a considered a mediating factor. Nonetheless, we have assessed the level of anxiety (and depression) in our ED participants. Fifth, we have not studied male patients with AN. Sixth, despite its extensive use in studies of ABMT, there is a discussion about the reliability of the dot-probe (Rodebaugh et al., 2016) and the measuring of response latencies as an index of AB (Christiansen et al., 2015). Moreover, some studies (Price et al., 2015), have shown limits in dot-probe measures as used in our study. Nonetheless, the use of the dot probe method here relies on the standard parameters conducted by the 'TAU-NIMH ABM Initiative' (http://people.socsci.tau.ac.il/mu/anxietytrauma/research/), that has been tried, tested and published on thousands of subjects in different age groups - children, teenagers and adults (Abend, Pine, & Bar-Haim. 2014). Last, as our sample has included only inpatients with, likely severe AN, our findings cannot be generalised to less severe forms of AN.

Despite these limitations and negative results, our study has several important advantages. It is a large-scale, hypothesis-generated RCT of carefully-selected patients with AN, using tools that have been previously used in the study of patients with EDs and anxiety disorders. In addition, it is of note that the participants did not receive psychotropic medication during the study period.

7 | CLINICAL IMPLICATIONS

To the best of our knowledge, this is the first study to investigate ABMT in both adolescent and adult patients with AN, assessing both ED-related and general/social anxiety-related threat stimuli in the same experiment. Our results add to the mixed findings in the study of ABMT in EDs, suggesting that it might not be beneficial in inpatients with AN receiving other treatment modalities at the same time. The intervention might be more applicable in outpatients with AN, who would likely not receive other treatments. Our findings further suggest that necessary adjustments in the ABMT paradigm should be considered before reaching definite conclusions about its efficacy in EDs.

8 | FUTURE DIRECTIONS

Future research is needed to better understand the underlying theoretical mechanisms of ABMT. As suggested by Mercado et al. (2020), establishing a solid theoretical understating may reduce the risk of heterogeneous training designs and lead to suitable training of the respective target populations. ABMT might be specifically applicable for outpatients with AN with improvement of their ED symptoms, who still show elevated anxiety despite previous other treatments provided. The study design ought to include a control group completing ACT. The inclusion of social appearance threat stimuli might be specifically applicable. Last, it might be beneficial to separate the applied stimuli and train adolescents with AN with pictorial stimuli, and adults with AN with linguistic stimuli.

AUTHOR CONTRIBUTIONS

Hadar Dikstein: Distributed the different psychometric batteries, was responsible for the Attention Bias Modification Treatment (ABMT), and wrote the article. Tal Gilon-Mann: Conceived and conceptualised the idea of the study, planned the study and its methodology, wrote the initial proposal, distributed the different batteries, and was responsible for the ABMT. Roni Halevi-Yosef distributed the studies questionnaires, and was responsible for patients' recruitment. Adi Enoch-Levi: Was responsible for the diagnostic assessment of all adolescent patients. Sami Hamdan: Conceived and conceptualised the idea of the study, and planned the study and its methodology. Eitan Gur: Was responsible for the diagnostic assessments of all adult patients. Yair Bar Haim: Conceived and conceptualised the idea of the study, constructed the original ABMT for patients with anxiety. Amit Lazarov: Constructed the original ABMT for patients with anxiety. Janet Treasure: Conceived and conceptualised the idea of the study, constructed the original ABMT for patients with anorexia nervosa. Daniel Stein: Conceived and conceptualised the idea of the study, was responsible for the diagnostic assessment of all adolescent patients, wrote the article. All authors read all the versions of the article, and contributed important ideas.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

PATIENT CONSENT STATEMENT

All patients and their parents (in the case of minors under age 18) agreed to participate in the study by signing a written informed consent after receiving an explanation about the aims and procedures of the study.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Not applicable.

CLINICAL TRIAL REGISTRATION

The study is a psychometric assessment and treatment study and as such is not considered a medical clinical trial according to the regulations of the Sheba Medical Center.

CONSORT STATEMENT

The study adheres to all the requirements of a randomized control trial (RCT). This is stated in the title of the study and in the abstract. The design of the RCT, including group allocation and methods of randomisation and of blinding is described in detail in the methods section. There have been no changes in the design of the trial during the entire period of the study. Eligibility criteria of the participants (inclusion and exclusion criteria) are described in the participants' section in the methods. The settings and location where the data has been collected are described in the methods section. The interventions for each group is described with sufficient details. The outcome is clearly described in the results section. There have been no changes in the outcome measures during the study. The sample has included all female patients with AN hospitalized in the adolescent and adult inpatient departments at the Sheba Medical Center, Tel Hashomer, Israel between 01/01/15 - 01/10/20, fulfilling the inclusion and exclusion criteria of the study and agreeing to participate (n=154). The numbers of patients undergoing each intervention is described in each Table of the study. Forty-four patients have not completed the study. The reasons for not completing the study are described in the participants' section in the methods. Accordingly: Forty-four participants dropped-out from the study either because of being released from the hospital before undergoing all the ABMT trials ($n = 25$), or because of wising to end the study prematurely ($n = 19$). The final sample has included 110 patients. None of the patients taking part in the study has experienced any harm or unwanted effects. As note

earlier, the study has not funded. The flow chart of the study us described in Figure 2.

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