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Short- and long-term effects of a randomized controlled trial

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Online attentional bias modification training targeting anxiety and depression in unselected adolescents: Short- and long-term effects of a randomized controlled trial

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Based on information processing models of anxiety and depression, we investigated the efficacy of multiple sessions of online attentional bias modification training to reduce attentional bias and symptoms of anxiety and depression, and to increase emotional resilience in youth. Unselected adolescents (N = 340, age: 11 – 18 years) were randomly allocated to eight sessions of a dot-probe, or a visual search-based attentional training, or one of two corresponding placebo control conditions. Cognitive and emotional measures were assessed pre- and post-training; emotional outcome measures also at three, six and twelve months follow-up. Only visual search training enhanced attention for positive information, and this effect was stronger for participants who completed more training sessions. Symptoms of anxiety and depression reduced, whereas emotional resilience improved. However, these effects were not especially pronounced in the active conditions. Thus, this large-scale randomized controlled study provided no support for the efficacy of the current online attentional bias modification training as a preventive intervention to reduce symptoms of anxiety or depression or to increase emotional resilience in unselected adolescents. However, the absence of biased attention related to symptomatology at baseline, and the large drop-out rates at follow-up preclude strong conclusions.

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Anxiety and depression are among the most prevalent psychiatric disorders and show a considerable increase during adolescence (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). Given the detrimental influence on later functioning, prevention and early intervention are of paramount importance. For this purpose, online cognitive training might be a potentially fruitful approach, especially for adolescents, given its low barriers, low costs, and anonymity. Also, adolescence is not only a period of increased vulnerability for emotional disorders, but also of heightened plasticity and potentially greater opportunities to profit from cognitive training (Crone, 2009).

There is ample evidence indicating that anxiety and depression are associated with the tendency to selectively attend to negative or threatening information: an ‘attentional bias’ (for meta-analyses see Bar-Haim, Lamy, Ergam PAS, Bakermans-Kranenburg, & van IJzendoorn, 2007; Peckham, McHugh, & Otto, 2010). Although most of this research is focused on adults, research in youth suggests that attentional bias is also related to clinical anxiety in children (Dudénye, Sharpe, & Hunt, 2015; Puliafito & Kendall, 2006), and to levels of depressive symptomatology in adolescents (Platt, Waters, Schulte-Koeve, Engelmann, & Salemink, in press). The role of attentional bias in non-clinical samples is less clear, with recent studies in adolescent community samples reporting either the presence (Platt, Murphy, & Lau, 2015) or absence (O’Leary-Barrett et al., 2015) of a relation between attentional bias and anxiety and/or depressive symptoms. As attentional bias seems to play an important role in the etiology of anxiety and depression (e.g., Van Bockxstaele et al., 2014), it seems a highly relevant target for early, preventive interventions. When adolescents would be able to adopt a positive information processing style, this might increase their emotional resilience (e.g., boost self-esteem or reduce negative thinking) and protect them against future development of anxiety.

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or depressive symptoms.

Various training paradigms have been developed that specifically target attentional bias, so-called Cognitive Bias Modification of Attention (CBM-A), with promising effects on cognitive and emotional functioning (for a review see: Kuckertz & Amir, 2015). The task employed most often is the dot-probe training (MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002). In that task, participants respond to a probe (often one or two ‘dots’) that replaces a neutral (or positive) stimulus which is presented simultaneously with a threatening (or negative) stimulus, thus encouraging attention to the non-threat location. Apart from mixed findings with the dot-probe training task (e.g., Heeren, Mogoae, Philipot, & McNally, 2015), qualitative studies suggest that credibility and acceptability of this type of attention training is quite low, as participants find it boring and miss a clear rationale (Beard, Weisberg, & Primack, 2011; Brosan, Hoppitt, Shelfer, Silience, & Mackintosh, 2011). A potentially more appealing alternative CBM-A paradigm is the visual search training (Dandeneau & Baldwin, 2004), where a single positive face has to be found in a 4 x 4 matrix of negative emotional faces. Here, both engagement with positive stimuli and disengagement from negative stimuli are trained during each trial. In a series of experiments, positive effects of this type of training have been observed on self-esteem and stress-responses in healthy adults (Dandeneau, Baldwin, Baccus, Sakellaropoulou, & Pruessner, 2007).

Thus far most studies on the efficacy of CBM-A as an intervention to reduce stress-reactivity, anxiety, or depression have focused on adult (mostly clinical) samples, and have provided mixed results (for meta-analyses see Cristea, Kok, & Cuypers, 2015; Heeren et al., 2015; Linetzkyy, Pergamin-Hight, Pine, & Bar-Haim, 2015; Mogoae, David, & Koster, 2014). One of these meta-analyses indicated larger effects on attentional bias and anxiety in younger participants (Mogoae et al., 2014), which fits with theories on increased vulnerability but also plasticity in youth (Haller, Cohen Kadosh, Scerif, & Lau, 2015). The number of studies in youth is now accumulating (for a review in the context of anxiety, see Lowther & Newman, 2014), but studies testing the efficacy of CBM-A in adolescents specifically remain scarce.

A meta-analysis on the first set of youth CBM-A studies (Cristea, Mogoae, David, & Cuypers, 2015, K = 9) showed that although moderate and significant training effects on attentional bias have often been reported, overall training effects on mental health were small and non-significant. Although these meta-analytic results suggest that CBM-A might not be suitable for preventive or clinical application in youth, it is important to note that CBM-A meta-analyses report large heterogeneity in effect sizes as well as in tasks, samples and outcome measures. For example, most of the CBM-A studies included in Cristea, Mogoae, et al. (2015) used the dot-probe training and (sub-)clinical samples, so more research is needed to increase insight into the effectiveness of specific training paradigms in various subgroups in youth, including non-clinical samples. With regard to CBM-A in unselected youth specifically, three previous studies report inconclusive findings. Changes in attentional bias have been observed in healthy children (Eldar, Ricon, & Bar-Haim, 2008) and unselected adolescents (de Voogd, Wiers, Prins, & Salemink, 2014), but not when visual search training effects were measured with a dot-probe assessment task (Platt et al., 2015). In unselected adolescents, the visual search training also reduced social anxiety symptoms (de Voogd et al., 2014), but not depressive symptoms (Platt et al., 2015; de Voogd et al., 2014). However, these earlier studies employed only one or two training sessions and did not include any follow-up assessments.

When evaluating the results of CBM-A studies in terms of emotional effects, it is important to take into account whether attentional bias was successfully manipulated. Based on the hypothesized causal role of attentional bias in anxiety and depression, the assumed working mechanism of CBM-A is a reduction in attentional bias for negative information. Therefore, a change in emotional functioning would only be expected if such an attentional bias reduction is obtained (MacLeod & Clarke, 2015). This implies that a change in attentional bias is the hypothesized mediating process, and some studies indeed found such a mediational role of attentional bias (Dennis & O’Toole, 2014; Kuckertz et al., 2014; Wells & Beeser, 2010). However, no significant mediation effects were found in a recent meta-analysis (Mogoae et al., 2014). It has also been suggested that increased attentional control might mediate the effects of CBM-A on emotional vulnerability (e.g., Klumpp & Amir, 2010). Attentional control, the ability to focus and switch attention, appears to be a protective factor against anxiety and depression (cf. Sportel, Nauta, De Hullu, De Jong, & Hartman, 2011). Assessing change in both attentional bias and attentional control is important to shed light on the mechanisms of change during CBM-A. These insights might also help in predicting for whom training might work best, that is, whether CBM-A is especially indicated for adolescents with a relatively strong attentional bias (Kuckertz et al., 2014) or low levels of attentional control (cf. Salemink & Wiers, 2012).

In the adult literature, many of the positive effects have been observed in clinical samples, mainly social anxiety patients (Linetzkyy et al., 2015; Mogoae et al., 2014). In non-clinical samples, there may be less room for improvement with regard to symptomatology, but research also suggests that CBM-A especially affects stress-reactivity (Hallion & Ruscio, 2011; Mogoae et al., 2014), which is also highly relevant for healthy or vulnerable adolescents with an eye on preventive purposes. As it might take time to generalize a newly acquired information processing style to daily life and the experience of stressful life events, emotional effects might only become apparent at a later time point (cf. Harmer, Goodwin, & Cowen, 2009). To assess whether CBM-A indeed has delayed effects on emotional functioning, and thus to fully appreciate its potential as a preventive intervention, long-term follow-up assessments are essential. Recent meta-analyses of CBM-A for social anxiety disorders in adults reported conflicting findings regarding long-term effects (up to four months); Linetzkyy et al. (2015) found some small effects, while effects were non-significant in Heeren et al. (2015). The only previous study investigating CBM-A as an early preventive intervention in adolescents with heightened social- or test-anxiety symptoms found no long-term effects on anxiety (Sportel, de Hullu, de Jong, & Nauta, 2013), but here CBM-A was combined with other forms of CBM and no consistent change in attentional bias was observed either. Note that the number of studies including follow-up assessments is still limited, especially in youth, and none of these earlier studies focused on non-clinical samples. Although not all adolescents are at risk for anxiety or depression, given the high prevalence of these disorders and potential stigma associated with indicated programs, universal prevention might effectively target many adolescents who might otherwise remain unnoticed (Farrell & Barrett, 2007). Furthermore, as the associated costs and time investments of CBM-A are relatively low, providing this training to unselected samples might be worthwhile.

The aim of the current study was to investigate the short- and long-term effects of two types of multi-session CBM-A in unselected adolescents. Adolescents were randomized over one of two

1 Note that this meta-analysis also included studies on CBM for interpretation (CBM-I, K = 14), which limits the possibility to draw conclusions on efficacy and moderators of CBM-A specifically.
experimental groups (dot-probe (DP) or visual search (VS) training) or one of two corresponding placebo control groups, and received eight sessions of online training over four weeks. Short-term effects on cognitive measures of attentional bias and attentional control (hypothesized mediators) and on stress-reactivity were assessed. Primary outcomes of anxiety and depression, and secondary outcome measures of emotional resilience were assessed pre- and post-training, and at three, six, and twelve months follow-up. Our first hypothesis was that both VS and DP training would result in reduced attentional bias and increased attentional control compared to the placebo training. Our second hypothesis was that VS and DP training would also result in reduced symptoms of anxiety and depression and increased emotional resilience compared to placebo. To examine factors that might affect training effectiveness (moderators), we tested whether stronger training effects are observed in adolescents who completed a relatively large number of training sessions (cf. Mobini, Reynolds, & Mackintosh, 2013), and in more vulnerable adolescents, i.e., those with a relatively strong attentional bias or low attentional control at baseline, or those who experienced more (impact of) stressful life events. Finally, we tested whether larger reductions in anxiety or depression would be observed for participants who showed a relatively larger reduction in attentional bias.

1. Methods

1.1. Design and ethics

The current study was part of a large scale multi-center, stratified, double-blind, placebo-controlled, parallel-group study conducted in The Netherlands (registered in the Dutch trial register with number NTR3950; http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=3950). Participants were randomized by a fully computerized procedure over eight parallel conditions, in a 4:4:4:4:1:1:1:1 ratio, with four experimental and four placebo computerized procedure over eight parallel conditions, in

1.2. Participants

Adolescents aged 11–18 were recruited from 14 regular high schools in The Netherlands, between January and September 2013. Inclusion criteria were: students in the 1st to 6th grade of a regular high school (all levels except special education) and parental consent. Of the 2312 adolescents who were invited, 733 participants and their parent provided written informed consent, registered and were randomized (see Fig. 1 for flow diagram). Four participants who dropped out wanted their data to be removed and were excluded from all analyses. Another 48 participants missed the pre-training assessment and were also excluded. Of the remaining 681 participants in the full study, 53 participants missed the post-training assessment, and five participants encountered technical problems during training or did not follow instructions, but all were kept in the analyses. For the current study on CBM-A, 340 participants (57.6% female, mean age = 14.41, SD = 1.20) remained for intention-to-treat analyses

1.3. Training paradigms

All training (and assessment) tasks were programmed in Adobe Flash (ActionScript 3.0).

1.3.1. Visual search attention training

The VS training was based on Dandeneau et al. (2007) with some adaptations for adolescents (de Voogd et al., 2014). In this task, participants had to find and select the single happy face in a 4 × 4 grid of negative emotional faces (sad, angry, and fearful; 5 each). To start a trial, participants had to move the mouse cursor over a fixation cross in the center of the screen. The faces were then presented until the participant responded. In case of an erroneous response the trial was repeated after feedback. The task consisted of four blocks with 36 trials each. A progress bar indicated how many trials were left in each block. Between blocks, short breaks were provided with feedback, consisting of the number of points earned based on performance (1–10 points based on RTs for correct trials). At the end of each session, points of this and, if applicable, previous session(s) were presented in a graph. We expected this feedback to improve motivation and engagement (cf. Garris, Ahlers, & Driskell, 2002). Face stimuli (height 149, width 117 pixels) were randomly drawn from two sets (counterbalanced over participants) of 36 adolescent faces (18 happy, six fearful, six angry and six sad faces) from the NIMH Child Emotional Faces Picture Set (NIMH-CEFS, Egger et al., 2011, for stimulus selection, see de Voogd et al., 2014). In the VS placebo condition, participants had to find and select the only 5-petaled flower in a 4 × 4 grid of 7-petaled flowers (Dandeneau et al., 2007). Other aspects of the task were identical to the experimental condition. The VS training took approximately 15 min to complete.

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2 In addition to the CBM-A training, the full study also investigated interpretation bias training and emotional working memory training. Since including all conditions and measures in one paper would compromise consistency and readability, these data are presented in separate papers (de Voogd, Wiers, De Jong, Zwitser, & Salemink, 2016; de Voogd, Wiers, Zwitser, & Salemink, in press).

3 Short-term analyses were also performed for ‘completers’, defined as having both T1 and T2 and six or more training sessions completed. In the current manuscript, only ITT analyses are reported, but results of the ‘completers’ analyses can be requested from the first author.
1.3.2. Dot-probe attention training

The original Dot-Probe (DP) training (MacLeod et al., 2002) was modified for use in child anxiety studies (TAU-NIMH initiative\(^ 4\); for details see http://people.socsci.tau.ac.il/mu/anxietytrauma/files/2013/08/TAU-NIMH-ABMT-Project-Overview.pdf, e.g., Bechor et al., 2014). Participants were presented with 160 trials, in which after presentation of a fixation cross in the center of the screen, two faces (height 143, width 191 pixels) from the same actor (angry or neutral) were shown on the top and bottom of the screen for 500 ms. Faces from 12 adult actors (six men) from the Nim-Stim stimulus set (Tottenham et al., 2009) were used and divided over two sets (counterbalanced over participants). In 120 trials an angry-neutral combination was shown, while the remaining 40 trials were neutral-neutral, to obscure the training contingency. After the 500 ms face presentation, a probe (“<” or “>”) appeared in the location of one of the faces. Participants had to respond with the corresponding arrow key on the keyboard as quickly as possible. The probe was presented until the participant responded. Actor, angry face location and probe direction were fully counterbalanced.

In the experimental condition, the probe location was always the location of the neutral face in angry-neutral trials. In neutral-neutral trials, this probe location was random. In the DP placebo condition, actor, angry face location, probe direction and probe location were all fully counterbalanced. Hence, there was no contingency between the location of the probe and the location of the negative and neutral stimuli. The DP training took approximately 8 min to complete.

\(^4\) We participate in this international collaborative project with our data on the DP training. Specifications of this training and the DP assessment task were prespecified and are identical at all participating sites. Therefore, we could not include feedback or a progress bar as in the VS training.

1.4. Cognitive outcome measures

The Emotional Visual Search Task (EVST) was developed by de Voogd et al. (2014), based on the VS training, to assess attentional bias. The assessment task largely resembled the VS training, but consisted of two blocks of 36 trials, where participants had to repeatedly select either the only happy face in a 4 × 4 grid of negative faces or the only face with a negative emotion (angry, fearful or sad) in a grid of happy faces. The order of positive or negative blocks was counterbalanced over participants. The same stimuli were used during T1 and training, while at T2 new stimuli were presented (stimuli sets counterbalanced over participants). An attentional bias index was computed by subtracting the average RT for selecting negative faces from the average RT for selecting positive faces.

The Dot-Probe attentional bias assessment task (DPT) was almost identical to the DP placebo training (for details on stimuli size, positioning etc., see Abend, Pine, & Bar-Haim, 2014). However, 120 instead of 160 trials were presented, with 80 neutral-angry trials and 40 neutral-neutral. Actor, angry face location, probe direction and probe location were all fully counterbalanced. The same face set was used at T1 and T2, while during training another set was presented. An attentional bias index was computed by subtracting average RT for congruent angry-neutral trials (probe at angry location) from incongruent angry-neutral trials (probe at neutral location).

1.5. Primary outcome measures

Anxiety symptoms were assessed with the Screen for Child Anxiety Related Emotional Disorders (SCARED, Birmaher et al., 1999), a 41-item self-report questionnaire assessing social phobia,
Depression Inventory (CDI, Kovacs, 1985), a 27-item self-report questionnaire that assessed the presence (scored 1) or absence (scored 0) of depressive symptomology (0–2). Cronbach’s alpha α = .86 in the current sample.

1.5. Motivation and performance

The Motivation Test for Children (PMT-K, Hermans, 1983). Only the competitive, intrusive and difficult to disengage from (test or social) performance motivation test for children (Prestatie Motivatie Test voor Kinderen, PMT-K, Hermans, 1983). Only the subscale assessing negative anxiety was used, consisting of 14 items that assessed the presence (scored 1) or absence (scored 0) of anxiety in various (test or social) performance situations. Cronbach’s alpha α = .81 in the current sample.

The Strengths and Difficulties Questionnaire (SDQ, Goodman, 1997) is a self- and parent-report questionnaire assessing emotional problems, conduct problems, hyperactivity-inattention and peer problems as well as pro-social behavior. The total difficulties score, computed based on all problem subscales, was used in this study. The questionnaire consists of 25 items, rated on a 3-point scale (0–2: not true – certainly true). Cronbach’s alpha α = .71 for self-report and α = .71 for parent-report in the current sample.

The Attentional Control Scale (ACS, Derryberry & Reed, 2002) was used to assess (subjective) attentional control. This 20-item (1–4 scale) self-report questionnaire assesses both attentional focusing and attentional shifting. Cronbach’s alpha α = .86 in the current sample.

Stress reactivity was assessed by using Cyberball (Williams, Cheung, & Choi, 2000; Williams, Yeager, Cheung, & Choi, 2012) as a social stressor. In this task, participants are led to believe that they play an online ball-tossing game with two other participants and are instructed to imagine this scene as vividly as possible. The 3-min game was programmed such that after two own tosses, the participant was excluded from the game. To assess changes in mood in response to the stress-task, before and after the task, participants had to indicate how anxious, nervous, sad, happy, confident, and enthusiastic they felt on a scale from 0 to 100 (not at all – very much). Ratings were combined into a positive and negative mood scale, respectively; these scales were analyzed separately, since previous CBM studies found differential effects on either positive or negative mood (e.g., Lothmann, Holmes, Chan, & Lau, 2011; Rohrbacher, Blackwell, Holmes, & Reinecke, 2014). In the current sample, Cronbach’s alpha α = .72 and α = .65 for positive and negative mood, respectively.

1.6. Secondary outcome measures

Self-esteem was assessed with the Rosenberg Self-Esteem Scale (RSES, Rosenberg, 1965), a 10-item self-report questionnaire with either positively or negatively stated items, rated on a 4-point scale (1–4). Cronbach’s alpha α = .86 in the current sample.

The Perseverative Thinking Questionnaire (PTQ, Ehring et al., 2011) was used to assess perseverative negative thinking. The PTQ is a 15-item self-report questionnaire with a 5-point scale (1–5) assessing key features of repetitive negative thinking (repetitive, intrusive and difficult to disengage from) and the unproductiveness of and mental capacity captured by this thinking. Cronbach’s alpha α = .95 in the current sample.

Test anxiety was assessed with a Dutch self-report questionnaire, the performance motivation test for children (Prestatie Motivatie Test voor Kinderen, PMT-K, Hermans, 1983). Only the subscale assessing negative anxiety was used, consisting of 14 items that assessed the presence (scored 1) or absence (scored 0) of anxiety in various (test or social) performance situations. Cronbach’s alpha α = .81 in the current sample.

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1.7. Stressful life events

Stressful life events were assessed with the Dutch ‘TRAILS Gebeurtenissen vragenlijst’ (Bouma, Ormel, Verhulst, & Oldehinkel, 2008), a self-report questionnaire assessing the occurrence and impact of 25 stressful events (e.g., parental divorce, severe illness/death of a family member, victimization). Participants had to indicate whether the event occurred either during the past 3 months, during the last 2 years or never/longer ago and how stressful (rated 0–3) the experienced event was. Impact scores for all experienced life events were added to create a stressful life events index, which was dichotomized into ‘high stress’ (>6) or ‘low or average stress’ for each time point. Finally, groups were created separating those who had ‘high stress’ at one or more time points and those who never had.

1.8. Procedure

Participating schools selected classes to invite, which were visited and instructed about the contents and aim of the study. The aim was explained as ‘investigating a training to make adolescents more resilient to stress and negative emotions, by learning to worry less and have a more positive view on your environment’. Information letters were also sent to the adolescents and their parents and both provided informed consent. The pre-training assessment (T1), the first training and the post-training assessment (T2) were all completed in computer rooms at school during regular school hours, under supervision of graduate students or the first author.

The parent version of the SDQ was sent by e-mail on the day of the pre- and post-training assessment and had to be completed by one parent within one week. The parent also reported on demographic characteristics (nationality, education) at T1. Assessments included four computer tasks5 (Self Ordered Pointing Task, DPT, Recognition Task, EVST), followed by online questionnaires (RSES, SDQ, SCARED, PTQ, PMT-K, CDI, life events,6 Alcohol Use Disorders Identification Test, and ACS for the adolescents, SDQ-P for parents). This procedure took about 80 min.

One to seven days after T1, the first training session was performed under supervision. The remaining seven training sessions were completed online at home, twice a week. Each session started with a reminder to have a quiet environment and no disturbances. Participants received a reminder by e-mail and text message and had two days to complete each session. Completion of training sessions was monitored by our online research system, and accuracy and RTs were registered. After missing two sessions, an e-mail was sent to remind them and offer technical assistance if needed.

At T2 (1–7 days after the last planned training session), the procedure from T1 was repeated and followed by Cyberball, before and after which participants completed mood scales. When all participants in a classroom were finished, they were fully debriefed on Cyberball and compensated for their participation. Compensation consisted of vouchers and participation in a lottery, with the value of vouchers and amount of lottery tickets based on the number of sessions completed (<six sessions: one lottery ticket; six or seven sessions: five euros and two lottery tickets; eight sessions: 10 euros & three lottery tickets). Three, six, and twelve months after the post-training assessment, participants and parents received an invitation for the online follow-up assessment (FU1, FU2 or FU3), including the same questionnaires as during T2. When the questionnaires were not completed, a reminder was sent after one week and non-responders were contacted by telephone after two weeks. Participants were compensated with vouchers (2.5 euros for each

5 Details on questionnaires and computer tasks that are not part of the current manuscript can be found in Supplement 1 in the supplemental material provided online.

6 Only assessed at T2 and follow-up.
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follow-up assessment).

1.9. Data analyses

For the EVST, incorrect trials (1.99% at T1; 1.75% at T2), correct repetitions of incorrect trials, and trials with RTs more than 2 SDs from the individual’s mean (4.28% at T1; 4.26% at T2) were removed before computing the attentional bias index (de Voogd et al., 2014). For the DPT, incorrect trials (4.47% at T1, 3.18% at T2) and trials with RTs more than 2.5 SDs from the individual’s mean (1.61% at T1; 1.79% at T2) were removed before computing the attentional bias index (cf. Bechor et al., 2014). For both the EVST and DPT, data of participants with an error rate 3 SDs above the mean error rate was excluded (n = 9 for EVST and n = 10 for DPT, all at T1). To examine whether the four groups differed on demographic characteristics or baseline scores on outcome measures, chi-square tests and ANOVA were performed.

To examine training effects, mixed regression analysis was performed (using IBM Statistical Package for Social Sciences 20), as this method takes into account all available data, without excluding participants with missing data at specific time points (which we assumed to be missing at random). For all outcome measures, a mixed model with Participant as the grouping variable and Time as a repeated measures variable was tested. School was not included as another grouping variable, as preliminary analyses indicated that this did not improve model fit and intra-class correlations were very small. With regard to the covariance between time points, we have verified (based on AIC and BIC criteria) whether these were structured according to compound symmetry, or first order autoregressive, or whether these were unstructured.

To test our hypothesis that VS training and DP training would reduce attentional bias, and anxiety and depressive symptoms and increase attentional control and resilience, the basic model for all outcome measures included the factorial predictors Condition, Type of training and Time, and their interactions. The factor Time had two levels for short-term outcome measures (T1 and T2), and five levels for long-term measures (T1, T2, FU1, FU2, and FU3). The best model was selected in a backward elimination procedure, in which parameters were excluded from the model based on AIC and BIC criteria and significance level of the parameters.

Potential moderators of training effects (number of sessions completed, baseline attentional bias, baseline attention control, stressful life events, and change in attentional bias) were analyzed separately for the VS and DP training. Difference scores were calculated for the attentional bias measures by subtracting pre-training scores from post-training scores and covariates were centered before including them in the analyses. To test our moderator hypotheses, separate models were tested including Condition, Time, the moderator of interest and their interactions. The effects of interest in these analyses were the three-way interactions between Condition, Time, and potential moderator.

For all analyses, Bonferroni-Holm correction was applied to control for Type 1 errors related to multiple comparisons. Effects with p < .05 that did not survive correction were defined as marginal. Statistics of the original and final models for all hypotheses can be found in Tables 4 and 6, and Table 5 shows the relevant parameters estimates (with the placebo condition, the DP type of training, and T1 as the reference categories).

2. Results

2.1. Preliminary analyses

At baseline (T1), groups did not significantly differ on demographic characteristics (see Table 1) nor outcome measures (see Tables 2 and 3), except for self-esteem scores, F (3, 338) = 2.84, p = .038, \( \eta^2_p = .025 \), with higher self-esteem for the DP and DP placebo group compared to the VS placebo group. Adding self-esteem as a covariate to our models did not affect relative model fit or the significance of any relevant parameters.

At T1, a significant attentional bias for negative information was found on the EVST, t (330) = 10.38, p < .001, d = 0.57, but not on the DPT, t (329) = 1.32, p = .188, d = 0.07. No significant correlations were observed between anxiety or depressive symptoms and attentional bias as assessed with the EVST, r = .05, p = .35, and r = .05, p = .36, respectively. For attentional bias as assessed with the DPT, a small and marginally significant correlation was observed with anxiety symptoms, r = .12, p = .03, but not with depressive symptoms, r = .05, p = .37. Scores on the EVST and DPT were not significantly correlated with each other, r = .042, p = .45.

On average, participants completed 5.33 (SD = 2.35) training sessions, and 82 adolescents (24%) completed all eight sessions. On average, participants completed their last training session 6.88 (SD = 6.48) days before the post-training assessment, with no significant difference between groups, F (3, 312) = 0.44, p = .723, \( \eta^2_p = .004 \). Accuracy rates during training were 99.1% for VS training, 98.7% for VS placebo, 97.5% for DP training, and 98.3% for DP placebo.

2.2. Cognitive outcome measures

Our first hypothesis, that VS and DP training would result in a reduction of negative attentional bias compared to VS and DP placebo, was partly confirmed. That is, for attentional bias as assessed with the EVST, a significant Condition \( \times \) Type \( \times \) Time interaction was observed (see Table 4), indicating a significant reduction in the VS training group only (see Table 5). For attentional bias as assessed with the DPT, the expected Condition \( \times \) Type \( \times \) Time interaction was not observed, nor any other main effects or interactions. For attentional control (ACS), the expected Condition \( \times \) Type \( \times \) Time interaction was also not significant. However, here a significant main effect of Time was observed, indicating an increase in attentional control irrespective of condition.

2.3. Primary outcome measures

Our second hypothesis, that VS and DP training would reduce anxiety and depressive symptoms, was not confirmed, as no significant Condition \( \times \) Type \( \times \) Time interactions were observed. Only significant main effects of Time were observed, indicating that anxiety and depressive symptoms generally reduced over time up till one-year follow-up.

2.4. Secondary outcome measures

The hypothesis that VS and DP training would increase emotional resilience was also not confirmed, as no significant Condition \( \times \) Type \( \times \) Time interactions were observed for any of the secondary outcome measures. Again, only significant main effects of Time were observed, indicating increased self-esteem and reductions in perseverative negative thinking, test anxiety, and

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7 As a first, broad step, potential training related effects in the full sample (including all experimental and placebo conditions) were assessed by looking at Condition (2: Experimental or Placebo) \( \times \) Training Type (4: VS or DP attentional training, interpretation training, or emotional working memory training) \( \times \) Time (pre- or post-training) interactions for all primary and secondary outcome measures. In the current manuscript, only CBM-A specific analyses are reported, but results of the overall analyses can be requested from the first author.
social-emotional and behavioral problems over time, irrespective of condition. With regard to stress-reactivity, we did not observe any significant changes in positive or negative mood in response to the Cyberball stress task, nor was mood affected by training condition (no significant main effects of Time and Condition, nor significant interactions).

2.5. Moderation of VS training

VS training effects on attentional bias assessed with the EVST were moderated by the number of completed training sessions, as indicated by a significant Condition × Time × Sessions interaction (see Table 6), such that the reduction of bias in the VS training group compared to VS placebo was larger for participants who completed more sessions, $B = -274.78, SE = 96.24, p = .005$. Attentional control did not moderate VS training effects on attentional bias, as no significant three-way interaction was observed. Nor were VS training effects on anxiety or depressive symptoms moderated by number of sessions completed, baseline attentional bias, baseline attentional control, or stressful life events. Also,
<table>
<thead>
<tr>
<th>Condition</th>
<th>Outcome measure</th>
<th>T1</th>
<th>T2</th>
<th>FU1</th>
<th>FU2</th>
<th>FU3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Visual search training</strong> (n = 125)</td>
<td>SCARED</td>
<td>19.04</td>
<td>13.09</td>
<td>16.31</td>
<td>12.44</td>
<td>16.23</td>
</tr>
<tr>
<td></td>
<td>CDI</td>
<td>8.89</td>
<td>6.24</td>
<td>7.49</td>
<td>5.22</td>
<td>7.32</td>
</tr>
<tr>
<td></td>
<td>RSES</td>
<td>29.87</td>
<td>5.45</td>
<td>30.46</td>
<td>5.44</td>
<td>31.79</td>
</tr>
<tr>
<td></td>
<td>PTQ</td>
<td>37.48</td>
<td>13.68</td>
<td>34.06</td>
<td>13.30</td>
<td>34.26</td>
</tr>
<tr>
<td></td>
<td>SDQ</td>
<td>10.32</td>
<td>5.18</td>
<td>9.54</td>
<td>5.31</td>
<td>9.09</td>
</tr>
<tr>
<td></td>
<td>SDQ-parent</td>
<td>6.75</td>
<td>4.71</td>
<td>6.19</td>
<td>4.65</td>
<td>5.91</td>
</tr>
</tbody>
</table>

| | CDI | 9.18 | 6.68 | 8.59 | 6.53 | 6.43 | 5.32 | 6.44 | 5.24 | 6.18 | 5.19 |
| | RSES | 29.08 | 5.54 | 29.65 | 5.18 | 31.67 | 4.89 | 31.68 | 4.89 | 31.56 | 4.95 |
| | PTQ | 34.18 | 10.85 | 34.85 | 13.67 | 35.21 | 10.08 | 32.63 | 12.12 | 32.22 | 11.94 |
| | PMT-K | 8.26 | 2.97 | 8.06 | 3.32 | 8.50 | 2.79 | 7.89 | 3.74 | 8.00 | 3.96 |
| | SDQ | 10.82 | 5.74 | 10.97 | 5.87 | 11.26 | 9.12 | 32.03 | 13.66 | 30.55 | 12.23 |
| | SDQ-parent | 6.36 | 4.11 | 6.25 | 3.27 | 6.68 | 4.38 | 5.74 | 4.23 | 5.78 | 4.56 |

| | CDI | 6.06 | 5.60 | 7.41 | 6.02 | 5.56 | 6.41 | 6.38 | 6.05 | 6.39 | 6.47 |
| | RSES | 31.05 | 4.80 | 31.89 | 5.09 | 31.60 | 5.51 | 32.64 | 5.17 | 32.10 | 5.15 |
| | PTQ | 35.17 | 12.64 | 32.44 | 12.23 | 31.26 | 12.93 | 32.03 | 13.66 | 30.55 | 12.23 |
| | SDQ | 9.69 | 4.88 | 9.22 | 5.10 | 8.02 | 4.95 | 7.61 | 4.85 | 8.29 | 5.21 |
| | SDQ-parent | 6.99 | 5.41 | 6.77 | 5.64 | 6.60 | 5.47 | 6.40 | 5.97 | 5.51 | 5.69 |

| **Dot-probe placebo** (n = 48) | SCARED | 18.23 | 12.17 | 16.38 | 12.28 | 13.46 | 10.86 | 12.48 | 11.46 | 15.45 | 13.11 |
| | CDI | 7.85 | 7.38 | 7.18 | 7.19 | 6.96 | 7.42 | 5.07 | 6.21 | 6.68 | 7.38 |
| | RSES | 31.67 | 5.20 | 32.02 | 5.89 | 31.86 | 6.81 | 33.85 | 4.55 | 33.18 | 5.47 |
| | PTQ | 32.21 | 11.50 | 30.31 | 12.35 | 31.00 | 13.24 | 28.11 | 11.79 | 30.14 | 13.79 |
| | PMT-K | 7.00 | 3.76 | 6.29 | 3.31 | 5.93 | 3.76 | 5.33 | 3.31 | 5.14 | 3.82 |
| | SDQ | 9.85 | 6.20 | 8.36 | 6.16 | 7.54 | 5.97 | 7.52 | 6.12 | 6.95 | 5.52 |
| | SDQ-parent | 5.79 | 5.14 | 5.90 | 5.80 | 4.94 | 6.09 | 4.57 | 5.28 | 4.39 | 4.67 |

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**Table 3**

Long-term outcome measures per training condition.

**Table 4**

Statistics of the original and final models.

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Note that most p-values between p < 0.01 and p < 0.05 are non-significant after Bonferroni-Holm correction.

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AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; EVST = Emotional Visual Search Task; DPT = Dot-Probe Task; SCARED = Screen for Child Anxiety Related Emotional Disorders; CDI = Children’s Depression Inventory; RSES = Rosenberg Self-Esteem Scale; PTQ = Perseverative Thinking Questionnaire; PMT-K = Performance Motivation Test for children; SDQ-P = Strengths and Difficulties Questionnaire (Parent); ACS = Attentional Control Scale.

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T1 = pre-training assessment; T2 = post-training assessment; FU1 = 3 months follow-up; FU2 = 6 months follow-up; FU3 = 12 months follow-up.
contrary to our expectations, training effects on anxiety or depression were not affected by change in attentional bias.

2.6. Moderation of DP training

DP training effects on attentional bias assessed with the DPT were not moderated by number of session completed, or baseline attentional control, as no significant three-way interaction were observed between Condition, Time and these variables. Nor were DP training effects on anxiety or depressive symptoms moderated by number of sessions completed, baseline attentional bias, baseline attentional control, or stressful life events. Also, contrary to our expectations, training effects on anxiety or depression were not affected by change in attentional bias.

3. Discussion

The aim of the current study was to investigate the short- and long-term effects of two types of multi-session CBM-A training in unselected adolescents. We hypothesized that both visual search

Table 6
Statistics of the original and unselected models – moderation analyses per training type.

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Modela</th>
<th>Model fit</th>
<th>Condition × Time × moderator</th>
<th>AIC</th>
<th>BIC</th>
<th>F</th>
<th>df</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attentional bias</td>
<td>Condition × Time (UN) × Sessions</td>
<td>5020.89</td>
<td>5061.82</td>
<td>8.15**</td>
<td>1,158.68</td>
<td>2976.42</td>
<td>3014.56</td>
</tr>
<tr>
<td></td>
<td>Condition × Time (CS) × Sessions</td>
<td>5039.42</td>
<td>5076.62</td>
<td>0.36</td>
<td>1,151.15</td>
<td>2933.10</td>
<td>2971.15</td>
</tr>
<tr>
<td></td>
<td>Condition × Time × ACS</td>
<td>3802.00</td>
<td>3952.53</td>
<td>2.67**</td>
<td>4,118.09</td>
<td>4106.95</td>
<td>4135.01</td>
</tr>
<tr>
<td>SCARED</td>
<td>Condition × Time × ACS</td>
<td>3732.18</td>
<td>3872.99</td>
<td>0.42</td>
<td>4,101.92</td>
<td>4056.59</td>
<td>4210.07</td>
</tr>
<tr>
<td></td>
<td>Condition × Time × EVST</td>
<td>3757.49</td>
<td>3908.02</td>
<td>0.14</td>
<td>4,102.18</td>
<td>4019.86</td>
<td>4263.81</td>
</tr>
<tr>
<td></td>
<td>Condition × Time × Stress</td>
<td>3678.38</td>
<td>3827.99</td>
<td>2.16</td>
<td>4,107.71</td>
<td>4075.65</td>
<td>4229.30</td>
</tr>
<tr>
<td></td>
<td>Condition × Time × EVST change</td>
<td>3471.75</td>
<td>3619.26</td>
<td>0.87</td>
<td>4,101.06</td>
<td>3897.61</td>
<td>4049.71</td>
</tr>
<tr>
<td>CDI</td>
<td>Condition × Time × Sessions</td>
<td>3036.99</td>
<td>3187.39</td>
<td>0.47</td>
<td>4,118.93</td>
<td>3361.33</td>
<td>3515.22</td>
</tr>
<tr>
<td></td>
<td>Condition × Time × ACS</td>
<td>2979.17</td>
<td>3128.85</td>
<td>0.74</td>
<td>4,986.66</td>
<td>3304.26</td>
<td>3457.56</td>
</tr>
<tr>
<td></td>
<td>Condition × Time × EVST</td>
<td>2997.03</td>
<td>3147.43</td>
<td>0.67</td>
<td>4,990.00</td>
<td>3295.06</td>
<td>3448.90</td>
</tr>
<tr>
<td></td>
<td>Condition × Time × Stress</td>
<td>2911.90</td>
<td>3061.38</td>
<td>1.08</td>
<td>4,100.51</td>
<td>3258.79</td>
<td>3412.28</td>
</tr>
<tr>
<td></td>
<td>Condition × Time × EVST change</td>
<td>2773.06</td>
<td>2920.44</td>
<td>0.28</td>
<td>4,978.84</td>
<td>3161.64</td>
<td>3313.55</td>
</tr>
</tbody>
</table>

<p>| Parameter estimates for significant effects compared to pre-training assessment. |
|-------------------------|--------|--------|--------|--------|--------|--------|</p>
<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Expa × VS - T2</th>
<th>T2</th>
<th>FU1</th>
<th>FU2</th>
<th>FU3</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>EVST</td>
<td>Condition × Type × Time</td>
<td>-1734.98***</td>
<td>276.97</td>
<td>-66.65</td>
<td>156.65</td>
<td>-</td>
</tr>
<tr>
<td>SCARED</td>
<td>Time</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CDI</td>
<td>Time</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>RSES</td>
<td>Time</td>
<td>-</td>
<td>-</td>
<td>0.57***</td>
<td>0.20</td>
<td>1.08***</td>
</tr>
<tr>
<td>PTQ</td>
<td>Time</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PMTK</td>
<td>Time</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.51***</td>
</tr>
<tr>
<td>SDQ-P</td>
<td>Time</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>ACS</td>
<td>Time</td>
<td>-</td>
<td>-</td>
<td>0.93**</td>
<td>0.29</td>
<td>-</td>
</tr>
</tbody>
</table>

\[ p < .10, * p < .05, ** p < .01, *** p < .001. \]

\[ ^a \] EVST = Emotional Visual Search Task; SCARED = Screen for Child Anxiety Related Emotional Disorders; CDI = Children’s Depression Inventory; EVST = Emotional Visual Search Task; DPT = Dot-Probe Task; ACS = Attentional Control Scale.

\[ ^b \] Bold = significant model (note that these models were tested after testing general training effects on primary outcomes measures, see Table 3), based on AIC and BIC and significance of parameters. Lower AIC and BIC values represent a better model fit.

\[ ^c \] UN = unstructured covariance; CS = compound symmetry. For SCARED and CDI, unstructured covariance was used for all models.
and dot-probe training would affect attentional bias, anxiety and depressive symptoms (primary outcomes), attentional control, and emotional resilience (secondary outcomes). Consistent with earlier research in youth (Waters, Pittaway, Mogg, Bradley, & Pine, 2013; de Voogd et al., 2014), VS attentional training led to an increased bias for positive information, as assessed with the closely matched EVST, but not with the DPT. This effect was most prominent in participants who completed relatively many training sessions. For DP training, no effects were found on attentional bias.

With regard to our primary outcome measures of anxiety and depressive symptoms, a long-term (one-year follow-up) reduction in symptoms was observed, but neither the VS nor the DP training outperformed their respective control conditions. The same pattern of results was observed for our secondary measures of emotional resilience. The absence of effects on symptomatology in combination with large effects on (visual search) attentional bias question the claim that absence of emotional effects can be attributed to failed manipulation of cognitive processes (MacLeod & Clarke, 2015). Given the cross-sectional and predictive associations between attentional bias and anxiety and depression, the lack of corresponding emotional effects might suggest that the current change in attentional bias mainly reflected that participants became better at the particular task (Srivastava, Mogg, & McEvedy, 2015). Consistent with such an explanation, there was no transfer between attentional bias tasks, and change in bias did not affect training effects on emotional outcomes. It has been suggested that CBM-A also might exert its positive effects on emotion through an increase in attentional control (e.g., Chen, Clarke, Watson, MacLeod, & Guastella, 2015; Klumpp & Amir, 2010), but we did not find such an effect on self-reported attentional control, neither did attentional control moderate training effects.

As symptoms of anxiety and depression were not correlated with EVST scores and only a weak correlation was observed between anxiety and DPT scores, one might also question the relevance of these attentional bias indices to symptomology in the current sample of unselected adolescents. In non-clinical samples, attentional bias might not be as strongly related to anxiety and depression as in clinical samples (O’Leary-Barrett et al., 2015), which would reduce the potential of CBM-A in this population. As previous research has shown that baseline attentional bias moderated training effects (e.g., Boettcher et al., 2013; Kuckertz et al., 2014), and the DPT did not reveal a baseline negative attentional bias, the lack of DPT bias change and corresponding emotional effects might thus be related to the absence of biased attention at baseline in this sample. Note that on the EVST, a bias for negative information was observed, but that the two assessment tasks differ on several aspects. One concerns the type of stimuli, with angry compared to neutral adult faces in the DPT and negative compared to positive adolescent faces in the EVST. Second, the DPT is a relatively implicit task, with short stimulus durations, while the EVST probably involves more strategic processes. It might be that the EVST better taps into relevant attentional processes of an unselected adolescent sample, and that enhancing a bias for positive information is more effective here (cf. Grafton, Ang, & MacLeod, 2012), instead of reducing a small or even non-existent negative attentional bias relative to neutral information. Furthermore, both reliability and convergent validity of the attentional bias measures used in our study have been criticized (Van Bockstaele, Salemink, Bögels, & Wiers, 2015). To assess training related changes, differentiating between various aspects of biased attentional processing and developing reliable indices of these processes is essential (see Iacoviello et al., 2014, and Zvieli, Bernstein, & Koster, 2015, for potentially fruitful approaches to optimize measurement of attentional bias).

Based on diathesis-stress theory (Beck, 1967), one would expect that changes in information processing primarily affect emotional functioning in interaction with stressful experiences (cf. Hallion & Ruscio, 2011; Mogg & Laibson, 2014). Therefore, an experimental stressor was included in the current study, but responses in terms of mood change were not affected by training condition. Also, long-term emotional effects might be observed, as newly acquired information processing styles could be applied in situations encountered after the training period (Harmer et al., 2009). However, the current results provide no support for this hypothesis, as long-term improvements in term of anxiety and depressive symptoms and emotional resilience were observed irrespective of training condition, and training effects were not moderated by stressful life events. Such a general improvement in emotional functioning is in line with previous findings on the development of anxiety and depressive symptoms (e.g., Sportel et al., 2013; de Voogd et al., 2016; de Voogd et al., in press). As mean symptom levels were already relatively low in our unselected sample, there might have been little room for improvement over and above natural decline or non-specific training effects. Stronger training effects might be obtained in (sub)clinical samples of adolescents, as research in clinically anxious children with variants of VS training also suggests (Waters et al., 2013; 2015).

Some limitations should be considered when interpreting the results of the current study. First, although our sample size was very large compared to previous research, response rates to our invitation for the study were modest and most adolescents did not complete all eight intended training sessions and all assessments. Apart from issues of representativeness, the low training compliance is a serious problem when considering implementation of CBM-A in prevention or treatment. Motivation for online training appears to be low in unselected adolescents, which is not surprising given the low levels of distress and the repetitive nature of the training tasks (Beard et al., 2011). Future studies should investigate how motivation and compliance can be improved, for example by adding game elements (cf. Notebaert, Clarke, Grafton, & MacLeod, 2015) or explaining the rationale of the training (cf. Beard et al., 2011; Brosan et al., 2011), although this could also undermine efficacy (Grafton, Mackintosh, Vujic, & MacLeod, 2014). A second limitation concerns the design of our control group. Initially, we planned to analyze our specific placebo groups together as one large control group. However, when reconsidering the limitations of this approach, we decided to treat the placebo groups as separate conditions. As a consequence, the control groups are smaller in size, which has reduced the power to detect training-related differences, especially in combination with the high drop-out rates at follow-up. Note that even though the placebo groups were much smaller than the experimental groups, their size was still adequate to detect small effects (of $f = 0.14$ with a power of 80%, and $p = .05$) post-training (where drop-out was minimal). Also, our VS placebo training might be criticized for the absence of exposure to emotional faces. However, a previous study comparing the VS and VS placebo training to an exposure-control condition showed that training effects could not be attributed to mere exposure (Dandeneau et al., 2007). A third limitation is related to the online nature of the training. While it has important advantages, the disadvantage is that training sessions were completed at home, without any supervision or standardization of training circumstances. Although accuracy rates (99% for VS training and 96% for dot-probe training) suggest that performance was not compromised, a lack of motivation and concentration (cf. Booth, Mackintosh, Mobini, Oztop, & Nunn, 2014 on the potential
negative effects of distraction), as well as technical issues, could all have played a role in the absence of expected training effects. Also, some suggest that a certain amount of stress might be beneficial, as it might improve training effects. The absence of (social) stress with online training at home compared to lab studies might explain recent null findings (Boettcher, Berger, & Renneberg, 2012; Boettcher et al., 2013; Kuckertz et al., 2014).

To summarize, this (to the best of our knowledge) first RCT assessing training effects of both visual search and dot-probe training in adolescents up to one-year follow-up, showed that VS training was effective in reducing attentional bias, while the DP training was not. However, primary and secondary emotional outcome measures revealed a general improvement in emotional functioning irrespective of condition. Although the attentional bias change obtained with online VS training performed at home seems promising, the current findings indicate that CBM-A in its current form is ineffective in reducing anxiety or depressive symptoms or increasing emotional resilience in unselected adolescents. More research is needed to investigate whether changes to the paradigms and/or methods of delivery might improve training efficacy, and to assess the potential of CBM-A in sub-groups of vulnerable (e.g., sub-clinical) adolescents.

Author contributions

R.W. Wiers, P.J.M. Prins, P.J. de Jong and E. Salemink developed the study concept and were involved in study design. W.J. Boendermaker programmed the EVST and VS training, and was involved in the design of these tasks. R.J. Zwitser was involved in data-analysis. E.L. de Voogd was involved in study design, collected data, performed data analysis and interpretation and drafted the paper, under supervision of E. Salemink. All authors contributed to the paper by providing critical revisions and they all have approved the final manuscript.

Declaration of conflicting interests

The authors declare that there are no conflicts of interest.

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