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PII: S0301-0511(15)30057-0
DOI: http://dx.doi.org/doi:10.1016/j.biopsycho.2015.09.008
Reference: BIOPSY 7095

To appear in:

Received date: 20-2-2015
Revised date: 19-8-2015
Accepted date: 21-9-2015

Please cite this article as: Sari, Berna A., Koster, Ernst H.W., Pourtois, Gilles, Derakshan, Nazanin, Training working memory to improve attentional control in anxiety: A proof-of-principle study using behavioral and electrophysiological measures.Biological Psychology http://dx.doi.org/10.1016/j.biopsycho.2015.09.008

Training working memory to improve attentional control in anxiety: A proof-of-principle study using behavioral and electrophysiological measures

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Highlights

- The effect of working memory training on attentional control is examined in high anxious individuals.
- Transfer effects were observed on distractor inhibition and attentional control (resting state EEG).
- Training related gains were related to lower levels of trait anxiety at post intervention.

Abstract

Trait anxiety is associated with impairments in attentional control and processing efficiency (see Berggren & Derakshan, 2013, for a review). Working memory training using the adaptive dual n-back task has shown to improve attentional control in subclinical depression with transfer effects at the behavioral and neural level on a working memory task (Owens, Koster & Derakshan, 2013). Here, we examined the beneficial effects of working memory training on attentional control in pre-selected high trait anxious individuals who underwent a three week daily training intervention using the adaptive dual n-back task. Pre and post outcome measures of attentional control were assessed using a Flanker task that included a stress induction and an emotional Antisaccade task (with angry and neutral faces as target). Resting state EEG (Theta/Beta ratio) was recorded to as a neural marker of trait attentional control. Our results showed that adaptive working memory training improved attentional control with transfer effects on the Flanker task and resting state EEG, but effects of training on the Antisaccade task were less conclusive. Finally, training related gains were associated with lower levels of trait anxiety at post (vs pre) intervention. Our results demonstrate that adaptive working memory training in anxiety can have beneficial effects on attentional control and cognitive performance that may protect against emotional vulnerability in individuals at risk of developing clinical anxiety.

Keywords: Working memory training; anxiety; attentional control

Introduction

Cognitive views on anxiety pose that deficits in attentional processes can causally contribute to the etiology and maintenance of anxiety (see Eysenck, 1992; Mogg & Bradley, 1998; Mathews & MacLeod, 2005 for reviews). Despite a wealth of findings and substantial progress in such research, it is still unclear whether attentional processes indeed play a causal role in anxiety (Van Bockstaele, Verschuere, Tibboel, De Houwer, Crombez, & Koster, 2014). In recent years, innovative methods have manipulated attentional processes to understand if there is a causal relationship between attentional processes and anxiety. So far, most research has focused on manipulating attentional bias which involves reducing exaggerated attention to fear-relevant information in anxiety (see Koster, Fox, & MacLeod, 2009). Based on theories of attentional control and anxiety (Eysenck, Derakshan, Santos, & Calvo, 2007) the current study is among the first to examine the effect of manipulating cognitive control on anxiety related distractibility and anxiety vulnerability at the behavioral and neural level. We start with a basic description of attentional control theory (ACT) and then explain the relevance of manipulating attentional control.

Attentional Control Theory

The attentional system can be divided into two sub-systems, a top-down (goal-directed, volitional) and bottom-up (stimulus-driven, reflexive) subsystem (Corbetta & Shulman, 2002). ACT (Eysenck et al., 2007) claims that anxiety impairs the balance between these subsystems by reducing the influence of top down, goal directed processes biasing the increased influence of bottom up, stimulus driven processes (Miyake, Friedman, Emerson, Witzki, Howerter, & Wager, 2000). Substantial evidence using a multitude of methods now shows that anxiety impairs the

efficiency by which the main central executive functions of working memory, namely the inhibition, shifting and updating of information, guide goal-directed behavior, reducing attentional control (see Derakshan & Eysenck, 2009; Eysenck & Derakshan, 2011; Berggren & Derakshan, 2013, for reviews). Extending the main assumptions of ACT (see Berggren & Derakshan, 2013), it seems that establishing a causal mechanism by which impaired attentional control can exacerbate anxiety's effects on performance outcome(s) through its emphasis on attention and maintenance on worrisome and ruminative thoughts, is imperative. A direct impact of reduced attentional control is the 'hidden' cost of compensatory processes that serve to maintain performance outcomes in high anxious individuals (e.g., Ansari & Derakshan, 2011a, Basten, Stelzel, & Fiebach, 2011, 2012; Righi, Mecacci, & Viggiano, 2009) exaggerating in turn the effects of anxiety on processing efficiency.

Recent theoretical accounts indicate a strong link between attentional control and working memory (see, Shipstead, Lindsey, Marshall, & Engle, 2014) as successful operation of working memory requires efficient use of attentional control in order to suppress task irrelevant information while processing goal-relevant information. Recent findings (e.g., Qi, Chen, Hitchman, Zeng, Ding, Li, & Hu, 2014) have confirmed the long standing assumption (see Derakshan & Eysenck, 1998) that anxiety is associated with reduced working memory capacity. Working memory can possibly mediate the relationship between anxiety and cognitive performance (Qi, Zeng, Luo, Duan, Ding, Hu, & Hong, 2014; Owens, Stevenson, Hadwin, & Norgate, 2012), with impairments in working memory capacity exaggerating the effects of anxiety on cognitive performance (Wright, Dobson, & Sears, 2014).

Manipulating attentional control

Adaptive cognitive training paradigms using the dual n-back training paradigm (Jaeggi, Seewer, Nirkko, Eckstein, Schroth, Groner, & Gutbrod, 2003) have been successful in improving a number executive processes such as general fluid intelligence (Au, Sheehan, Tsai, Duncan, Buschkuehl, & Jaeggi, 2014), inhibition and working memory capacity (Owens, Koster, & Derakshan, 2013) and cognitive control (Schweizer, Grahn, Hampshire, Mobbs, & Dalgleish, 2013), with training-related gains on untrained tasks measuring similar (near transfer) or different (far transfer) processes (but see Shipstead, Redick, & Engle, 2012). The adaptive dual n-back task is a working memory task where two streams of information – visual and auditory - need to be processed simultaneously. In this task, participants are asked to indicate whether there has been a match either for the visual or auditory information between the current trial and a number (*n*) trials back in the series. The task can get progressively more difficult with the level of '*n*' increasing as participant performance improves, thus providing an adaptive training. Such adaptive cognitive training techniques hold important implications for improving clinical outcome(s) in emotionally vulnerable populations. For example, Owens et al. (2013; see also Schweizer et al., 2013) using a dual n-back task investigated if training could improve cognitive control in individuals with sub-clinical levels of depression. Adaptive training and non-adaptive control groups underwent the intervention for eight days over a two week period. The adaptive training group's performance could increase in difficulty up to 4-back level while the non-adaptive control group only practiced the 1-back version of the task, without adaptation as a function of performance improvement. Training-related gains were found to transfer to behavioral and neural measures of working memory capacity and the efficiency of filtering of irrelevant information in the adaptive training compared to the control group. Other recent

findings have also shown benefits of cognitive training in improvements on cognitive control. For example, Siegle, Price, Jones, Ghinassi, Painter and Thase (2014) showed that cognitive control training can have beneficial effects on reducing rumination in clinically depressed patients. Furthermore, Cohen, Mor and Henik (2015) showed training related gains on state rumination using a cognitive control training task that emphasized distractor inhibition. Finally, a study by Bomyea and Amir (2011) demonstrated that cognitive control training led to decreased intrusive thoughts, a hallmark of affective disorders including anxiety disorders.

The Current Study

Most studies performed so far have examined the beneficial effects of cognitive control training in the context of depression. Provided the relevance of impaired attentional control in anxiety (cf. Eysenck et al., 2007), the current study sought to determine if daily training for 15 days distributed over a three weeks period on the adaptive dual n-back task can result in improved attentional control in preselected high anxious individuals low on different measures of attentional control (Derryberry & Reed, 2002). We included a training group and an active control group. The training group performed an adaptive dual n-back task and the control group performed a non-adaptive dual 1 back task. To examine transfer of training, pre and post intervention measures of attentional control included: A Flanker task measuring distractor inhibition, an Antisaccade task with emotional faces as target to assess attentional control and inhibition in relation to emotional material, and resting state EEG (Theta/Beta) ratio, an index of prefrontal cortex related attentional control (Putman, Verkuil, Elsa Arias-Garcia, Pantazi, & van Schie, 2014). We now describe the selection of this transfer in more detail.

The Flanker task (Eriksen & Eriksen, 1974) was based on a modified version used in Berggren and Derakshan (2013). In this task, two types of arrows (distracter arrow, target arrow) indicating right or left were presented. Participants were instructed to ignore the distracter arrows and indicate the direction of the target arrow. The Flanker task has been used extensively in the literature in studies where distractor inhibition has been investigated (Shipstead, Harrison, & Engle, 2012; Lavie, Hirst, de Fockert, & Viding, 2004). Since high working memory capacity has been found to eliminate the adverse effect of acute stress (Otto et al., 2013), the Flanker task also included a state anxiety manipulation of presenting loud bursts of white noise randomly in half of the blocks. State anxiety manipulations using white noise have previously found to be successful (see Rossi & Pourtois, 2014). Using this manipulation, we aimed to assess selective attention under challenging conditions where the need to address the task demands is considered to place greater challenges on working memory functions for high anxious individuals (see Derakshan & Eysenck, 1997; Berggren, Richards, Taylor, & Derakshan, 2013).

The Antisaccade task (Hallet, 1978) was based on Derakshan, Ansari, Hansard, Shoker and Eysenck (2009; Exp 2). This task is a well validated and extensively used measure of attentional control in normal (see Hutton & Ettinger, 2006; Ettinger, Ffytche, Kumari, Kathmann, Reuter, Zelaya et al., 2008) and emotionally vulnerable populations suffering from anxiety and depression (see Berrgren & Derakshan, 2013, for a review). During the Antisaccade task, participants are required to saccade towards (prosaccade) or away from (antisaccade) an abrupt peripheral target flashed on the screen, as quickly as possible. Anxiety has been associated with a slowing on antisaccade latencies requiring the efficient exercise of attentional control processes of working memory in relation to target inhibition (e.g., Ansari & Derakshan, 2010; 2011a, Derakshan et al., 2009; Exp 1), and when the targets were angry facial expressions of emotion

(Derakshan et al., 2009; Exp 2). Here, we used angry and neutral facial expressions as targets and were interested to observe training related gains on antisaccade latencies in relation to the inhibition of angry targets, predicting that training would result in faster antisaccade latencies especially for to-be-inhibited angry targets.

As a neurophysiological measure during the antisaccade trial, keeping with Ansari and Derakshan (2011a), we used Event Related brain Potentials (ERPs) focusing on the time window 50 ms prior to target presentation to observe if training affected changes in ERP activity in this interval which is known to predict antisaccade performance (Everling, Matthews, & Flohr, 2001). Ansari and Derakshan (2011a) previously found impaired performance efficiency during this interval as indexed by lower fronto-central negativity in high compared with low-anxious participants. Hence, given the sensitivity and reliability of this period in explaining antisaccade performance, we focused our analysis on this specific interval.

Resting state electroencephalography (EEG) as an alternative electrophysiological measure of trait attentional control was used. Via resting state EEG, we quantified neural activity in different frequency bands (i.e. theta band, 4-7 hz for slow oscillations; beta band, 13-30 hz for fast oscillations). Changes in power in these different frequency bands have been taken as an index of increased or decreased attentional control. For example, slow wave oscillation is mostly involved in stimulus driven processes whereas fast wave oscillation is related more to top down regulation of control and attention (Knyazev, 2007). Hence, an increased ratio between these two frequency bands was taken to indicate decreased cognitive or attentional control. For example, increased slow wave/fast wave ratio (SW/FW; theta/beta) is related to attentional problems such as Attention-Deficit/Hyperactivity Disorder (ADHD; Clarke, Barry, McCarthy, & Selikowitz, 2001; Arns, Conners, & Kraemer, 2012; but see Buyck & Wiersema, 2014b). Furthermore,

Buyck and Wiersema (2014a) showed that specifically the inattentive subtype of ADHDwas related to abnormal SW/FW over the life span. Additionally, SW/FW negatively correlates with self-reported attentional control (Putman, van Peer, Maimari, & van der Werff, 2010; Putman et al., 2014) confirming that the SW/FW index can be used as a valid neurophysiological marker or correlate of attentional control.

Predictions

We predicted that participants in the adaptive training group would show improvement in working memory performance throughout the training period. Secondly, we predicted that such training related gains would transfer to attentional control processes at the neurophysiological level, as measured by the SW/FW, as well as performance on the Flanker task as a behavioral measure of distractor inhibition and the Antisaccade task as a measure of inhibition both at behavioral and neurophysiological levels. Lastly, due to the close links between WM and attentional control (Shipstead et al, 2014) extensive WM training was expected to lead to improvements in attentional control and eventually reduction in trait anxiety levels.

Method

Participants

Participants were student volunteers recruited via advertisements from the campus of Birkbeck University, London. They were pre-selected on the basis of their elevated trait anxiety scores on the trait anxiety scale of the State-Trait Anxiety Inventory (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983; STAI-TA $\geq$ 50) and low scores on the Derryberry and Reed's (2002) attentional control scale (ACS $\leq$ 60). Derryberry and Reed (2002) showed that such individuals are most strongly biased to process negative information. Participants were semi-

randomly (the task started randomly either with the eyes open or closed condition and continued alternately) assigned either to the control (dual 1-back training: $N = 16$) or training (dual n-back training: $N = 17$) group. The training and control groups did not differ from each other on either STAI-TA (Control, $M = 57.81$, $SD = 5.52$; Training, $M = 60.18$, $SD = 8.43$; $t < 1$, *NS*) or ACS scores (Control, $M = 45.88$, $SD = 8.15$; for Training, $M = 43.65$, $SD = 7.18$; $t < 1$, *NS*) at baseline. The two groups had similar age (Control, $M = 26$, $SD = 5$; Training, $M = 25$, $SD = 6$; $t < 1$, *NS*) and gender distribution (Control, 2 males-14 females; Training, 6 males-11 females; $\chi^2(1, N = 33) = 2.33$, $p = .13$). Seven participants did not complete the study during the training without providing a reason (3 from control and 4 from training group). Participants were compensated 50 GBP, or given course credit for their participation.

Among the participants who completed the study, training and control groups also did not differ from each other either on STAI-TA scores (Control, $M = 57.92$, $SD = 5.53$; Training, $M = 60.92$, $SD = 8.68$; $t(24) = 1.05$, $p = .30$), ACS scores (Control, $M = 45.85$, $SD = 8.99$; Training, $M = 43.08$, $SD = 6.95$; $t < 1$, *NS*) at baseline, age (Control, $M = 26$, $SD = 5$; Training, $M = 23$, $SD = 5$; $t(24) = 1.51$, $p = .39$) or gender (Control, 1 males - 12 females; Training, 5 males - 8 females; $\chi^2(1, N = 26) = 3.47$, $p = .06$). At pre-intervention, training and control groups did not differ from each other on STAI-SA scores either (Training group, M = 47.62, SD = 10.17; Control group, M = 51.69, SD = 9.27, $t < 1$, *NS*).

Materials and Tasks

Self-report scales. Participants completed the State-Trait Anxiety Inventory (STAI-TA, STAI-SA; Spielberger et al., 1983), the Attentional Control Scale (ACS; Derryberry & Reed, 2002), and the Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec,

1990) at pre and post intervention in the lab. The STAI-TA, STAI-SA and ACS each contain 20 questions and are presented on a 4 point Likert type scale. PSWQ has 16 items and is presented on a 5 point Likert type scale. While the STAI-TA, ACS, PSWQ measure trait characteristics, the STAI-SA measures state characteristics. The main interest of the current study is on trait anxiety assessed via STAI-TA.

Resting State EEG. Resting state EEG was recorded during 8 one-minute long blocks of alternating eyes open or eyes closed conditions (cf. Putman, Arias-Garcia, Pantazi & van Schie, 2012). The task started either with eyes open or closed conditions and continued alternately. Starting block was randomly decided for each participant. Since brain activity during an open or closed eyes condition may differ, the mean activity between these conditions is recommended to be the most informative index (Barry, Clarke, Johnstone, Magee, & Rushby, 2007). Hence, power densities for the three frontal electrodes (F3, Fz, F4) were averaged across these two conditions. Slow wave oscillations were represented by theta, in the 4-7 Hz frequency band while fast wave oscillations were captured by beta, in the 13-30 Hz frequency band activity during this state. The ratio between frontal slow wave and fast wave (SW/FW) activity was calculated as an index of attentional control (see Putman et al. 2010, 2014), with higher scores indicating lower attentional control levels.

Flanker task. This task was a modification of the Flanker task used in Berggren & Derakshan (2013). Each trial started with a fixation cross for 500 ms. The distractor cues which were 2 sets of 2 arrows (<< or >>) appeared 3.1° above and below from fixation, pointing right or left (for a random duration between 12 to 26 ms depending on the monitor refresh rate -75 Hz. 98% of the time, duration was either 13 or 14 ms). Afterwards, a target arrow, which was a single set of 2 arrows pointing right or left, appeared in the middle of the screen. Participants were

instructed to ignore the distracting cues and indicate the direction of the target arrow. In half of the trials, both target and distractor cue arrows showed the same direction (compatible) and in the other half they showed opposite directions (incompatible). Upon starting the task, the participants were informed they might hear a loud white noise (103 dbA) during the task. In half of the blocks, the white noise (perceived as aversive) was randomly presented during the inter trial interval (noise blocks) and there was no noise in the other half of blocks (safe blocks). Participants were informed whether they would hear a white noise at the beginning of each block. On noise blocks the noise was presented on ~10% of the trials. There were 4 blocks in total, each including 72 trials. Starting block was randomly determined. Participants in the training and control group did not differ from each other in terms of the condition of the block they started with, χ^2 (1, N = 33) = 1.59, p = .30.

Antisaccade task. This task was based on Ansari and Derakshan (2011b) with angry and neutral facial expressions (Lundqvist, Flykt, & Öhman, 1998) serving as target. There were 16 experimental blocks (8 antisaccade and 8 prosaccade) each containing 40 trials. These two facial expressions were distributed evenly within blocks. After a short practice session, the experimental blocks started either with an antisaccade or a prosaccade block, and continued alternately. Each trial started with a fixation cross for a variable duration ranging from 2600 to 3600 ms, and participants were instructed to fixate the cross whenever on the screen. Shortly after the fixation cross disappeared (200 ms gap), a face (3.3° × 6°) appeared 11° away from the center of the screen either at the right or left side along the horizontal axis.

After a short practice session, the experimental blocks started either with an antisaccade or a prosaccade block, and continued alternately. On prosaccade blocks, participants were

instructed to look at the face and on antisaccade blocks, they were instructed to look away from the face to its mirror position on the screen as fast as possible without looking at it. Faces were presented for 600ms.

Adaptive Dual *n*- back Training Task. This online training task was similar to Owens et al. (2013) and based on the work of Jaeggi, Buschkuehl, Jonides, and Perrig (2008). Participants were presented a 3 by 3 grid with a fixation cross in the central cell (see Figure 1). A green square appeared in one of the remaining 8 cells. Five-hundred ms after the appearance of the square, a letter (c, h, k, l, q, r, s, or t) was spoken. Participants were asked to remember the position of the square and the letter spoken. If there was a match between the *n* trials back and the current one, they were asked to respond. If there was a position match, they pressed the "A" key on the keyboard. If there was a sound match, they pressed the "L" key. If both were matching, they were asked to press both keys. In case of no match, participants were instructed not to press any key. Each training session consisted of 20 blocks with 20 + *n* trial in each (for example, in a 2-back block there were 20+2=22 trials; in a 3 back block there were 20+3=23 trials). In each of the blocks, there were equal numbers of matches (4 for the position, 4 for the letter, 2 for both). Positions and the letter spoken were randomly distributed within the task. There were 15 seconds fixed breaks between blocks and participants could not terminate the task once it started. Each session lasted approximately 30 minutes. Level of task difficulty (*n*) increased depending on performance such that if accuracy on both the position and letter match was 95% or above, level of *n* increased by 1 in the following block. However, if accuracy rate was between 75% - 95%, participants continued with the same level. If their performance got worse (less than 75% accuracy), task difficulty decreased by one level of *n*. Participants were informed about the difficulty of the level in the beginning of each block.

Non-adaptive dual 1-back control task. The control group completed 20 blocks of dual 1-back trials across the training days regardless of their performance. Here, participants were asked to respond if there was either a position, letter (or both) match with the previous trial.

Accuracy rate per training block for each participant was recorded online and immediately visible to the experimenter, as performance of participants was routinely monitored remotely by the experimenter. If accuracy rates were lower than regular, the participant was contacted in due time by the experimenter. No noticeable difference between the participants in the control group and the training group were observed on adherence to the instructions on the time of training during this period.

Procedure

Prescreened participants were invited to the lab where they completed the STAI-TA, ACS and PSWQ. They were then prepared for EEG testing and resting state EEG was recorded. Participants then performed the Antisaccade task. Afterwards EEG equipment was removed and the experiment continued with the Flanker task (due to the concerns about the length of the experiment session, EEG was not recorded during the Flanker task). Participants completed the STAI-SA before and after the task for assessments of state anxiety before and after the stress manipulation via white noise.

Finally, participants were given an introduction to the training task and were able to practice a few trials with the experimenter in the lab for familiarization with the task and to ensure that they had understood the instructions correctly. They were told that they should complete the task for 3 weeks at approximately the same time every week-day. Participants were able to see a summary of their daily performance and progress after each session. Additionally, they were told that the experimenter would be tracking their performance and completion rates on

a daily basis. After the 3-week period, participants were invited back to the lab again for post-intervention measurements where they completed the same tasks and questionnaires as at pre-intervention.

EEG Data Acquisition

EEG data was recorded from 30 Ag/AgCl electrodes mounted in fitted cap (EASYCAP) according to 10/20 system (F3, Fz, F4, FC1, FC2, FC5, FC6, C3, Cz, C4, CP5, CP6, P3, Pz, P4). Electrode impedances were kept below 5kΩ. All electrodes were referenced on-line to the mean of left and right mastoids. Forehead was used as ground. Horizontal eye movements (HEOG) were recorded with electrodes placed on the outer canthi of the eyes and vertical eye movements (VEOG) were recorded from an electrode placed below the left eye. Data was amplified between 0.1 and 125 Hz, sampled at 1000 Hz and offline filtered with a bandpass frequency of 0.01-30 Hz for the Antisaccade task and 0.01-100 Hz for the resting state EEG. Data was automatically corrected for eye blinks and ocular artifacts. For the Antisaccade task, baseline correction was performed before and after ocular correction based on the pre-stimulus onset (300 ms). Artifact rejection criteria were set to ±90μV for the antisaccade task and ±100μV for the resting state EEG. After applying these criteria, at pre-intervention 79% and at post-intervention 83% of the resting state EEG data remained. For the antisaccade task, 12% of the data at pre-intervention and 6% of the data at post-intervention were removed due to artifacts.

Results

Performance on the Training and Control Dual n-back Tasks

Figure 2 shows performance improvement on the dual n-back task in the training group. Working memory performance improved as indicated by greater levels of difficulty attained towards the end of training from mean performance in the first three days of training (M = 1.85, SD = .58) to the last three days (M = 2.49, SD = 1.10), $t(12) = 3.57$, $p < .01$. By comparison, the control group showed 94% accuracy overall and their scores did not vary from the first *n*-back session (95%) to the last *n*-back session (95%).

Resting State EEG

Figure 3 shows the SW/FW EEG index for control and training groups at pre and post interventions, respectively. Data for 2 participants (1 from control, 1 from training) were lost during recording. Data were analyzed using a Mixed ANOVA with Time (pre-intervention, post-intervention) as within subjects factor and Group (Training, Control) as between subjects factor. There was no main effect of time, $F < 1$, but an interaction between Time and Group emerged, $F(1,22) = 4.90$, $p < .05$, that showed reductions in SW/FW from pre to post intervention in the training group (M =.11, SD = .22) that were greater than the changes observed in the control group (M = -.08, SD = .19), $t(22) = 2.21$, $p < .05$ who in fact even showed an increase in SW/FW. There were no group differences at pre- or post- intervention, both ts<1.

Flanker task

Data for 3 participants in the control group were discarded due to low accuracy rate (greater than 2.5 SD of the mean), slow reaction time (RTs slower than 2.5 SD) and extreme

stress due to loud bursts. Only RTs for correct trials were considered. RTs exceeding 3 *SD* of the individual mean scores were also discarded. The analyses were run on 92% of the total pre-intervention and 93% of the post-intervention data.

Consistent with Berggren and Derakshan (2013), we calculated interference scores by subtracting RTs on incompatible trials from RTs on compatible trials. Interference scores were subjected to a Time (pre, post intervention) X Group (Control, Training) X Condition (Safe, Noise) Mixed ANOVA. A main effect of time, $F(1,21) = 6.89$, $p < .05$ showed that interference scores were lower at post ($M = 74$, $SD = 30$) compared with pre-intervention ($M = 87$, $SD = 36$). There was a main effect of condition, $F(1,21) = 5.00$, $p < .05$, with greater interference scores for noise ($M = 84$, $SD = 35$) than safe blocks ($M = 77$, $SD = 29$), which was qualified by a time X condition interaction, $F(1,21) = 4.60$, $p < .05$, indicative of greater reductions in interference in the safe (86 vs 68, $t = 3.34$, $p < .01$) compared with the noise condition, (88 vs 79, $t = 1.45$, $p = .16$). This observation was corroborated by a three way interaction of time X condition X group, $F(1, 21) = 7.46$, $p < .05$, where the training group showed significant reductions in interference in both safe and noise conditions from pre to post-intervention (both ts > 2.48, ps $< .05$), whereas the control group only showed a marginally significant reduction in the safe block ($t = 2.18$, $p = .056$) but not in the noise block ($t < 1$, *NS*; see Figure 4) [1].

In order to assess state anxiety level during the Flanker task we averaged STAI-SA scores before and after the Flanker task. Time (pre, post intervention) X Group (Control, Training) mixed ANOVA led to significant main effect of time indicating lower scores at post-intervention ($M = 48.24$, $SD = 7.67$) as compared to pre-intervention ($M = 50.85$, $SD = 9.11$), $F(1, 21) = 6.86$, $p < .05$ but no interaction effect emerged $F(1, 21) = 2.29$, $p = .15$.

Antisaccade task

One participant's data was discarded due to the small percentage of accurate trials (2.5 *SD* lower than the mean). Analyses were run on correct saccades which were defined as the first saccade in the right direction after target onset (86% of trials at pre-intervention and 90% of trials at post intervention). Groups did not differ from each other either at pre or at post intervention in terms of correct saccades (all *t*s < 1, *NS*). In keeping with Ansari and Derakshan (2011b), saccades faster than 80 ms and slower than 500 ms were removed. Using Brain Vision Analyzer, leftward and rightward saccades were separated and the difference between the potentials of the left and right HEOG electrodes was calculated and saccades were identified as peaks. Peaks exceeding 50 μV on the correct/expected direction (polarity) were marked as valid saccades.

There were two main dependent variables: (i) Latencies of correct saccades, which were defined as the elapsed time between target onset and a saccade (i.e., peak in the HEOG) in the right direction, and (ii) central negativity, which was measured in the interval of 50 ms prior to target presentation, in line with Ansari and Derakshan (2011a) and Everling et al. (2001). Here, for central negativity, we averaged the activity of the electrodes at the central sites available (C3, Cz, C4).

Latencies. Group comparisons for the antisaccade latencies at pre-intervention was marginally significant for neutral trials (Control, $M = 269$, $SD = 37$; Training, $M = 244$, $SD = 25$), $t(23) = 2.00$, $p = .058$ and significant for the angry trials (Control, $M = 268$, $SD = 32$; Training, $M = 243$, $SD = 26$), $t(23) = 2.15$, $p < .05$, indicating slower reaction times for the control group as compared to the training group. Hence, analyses on the post-intervention antisaccade latencies were run separately for each emotional condition controlling for the baseline differences. ANCOVA with antisaccade latencies as a dependent variable, group (control, training) as a fixed factor and pre-intervention antisaccade latencies as a covariate

revealed no group differences for either of the conditions (neutral faces: control, M = 253, SD = 31; training, M = 221, SD = 31, F (1, 22) = 2.05, p = .17; angry faces: control, M = 252, SD = 28; training, M = 221, SD = 29, F (1, 22) = 2.32, p = .14).

For the prosaccade latencies, a Mixed ANOVA with Time (pre-intervention, post-intervention) and valence (neutral, angry) as within subjects factors and Group (Training, Control) as between subjects factor was run. There was a marginal valence x group interaction; F(1, 23) = 4.24, p = .051, indicating that the control group was slower on angry (M = 176, SD = 15) vs neutral trials (M = 175, SD = 15), as opposed to the training group who showed slower latencies on neutral (M = 167, SD = 13) compared to angry trials (M = 165, SD = 12). No other effect reached significance (Time x Group interaction, F(1,23) = 2.19, p = .153, all the other Fs < 1, *NS*.).

Central Negativity. Figure 5 shows the grand averaged waveforms for antisaccade trials pre to post intervention difference, for neutral and angry trials. A mixed ANOVA with Time (pre – post intervention) X Valence (angry, neutral) X Group (training, control) showed a significant main effect of Time, F(1,23) = 10.80, p < .01, indicative of a greater negativity at post intervention (M = -1.19, SD = 1.03) vs pre-intervention (M = -0.88, SD = .89). A trend effect of valence, F(1,23) = 3.23, p = .09, indicated greater negativity for angry (M = -1.14, SD = .92) vs neutral (M = -.93, SD = 1.03), and a marginal interaction between valence x time, F(1, 23) = 2.98, p = .10, with a greater increase in negativity for neutral faces (-.7 vs -1.16) vs angry faces (-1.06 vs -1.23) were found. The three way interaction of time X valence X group, F(1, 23) = 5.43, p < .05, revealed that the control group had greater increase in negativity (Mdiff = -0.78; t = 3.77, p < .01) on neutral trials, and no increase on angry trials, t < 1. The training group on the other hand showed

a marginal increase on angry trials (*M*diff = -.24; $t = 1.85$, $p = .08$, two tailed), and no increase on neutral trials, $t < 1$.

Self-reported Symptomatology

Separate mixed ANOVAs for each scale (ACS, PSWQ, STAI-TA) with time (pre-intervention, post-intervention) as within subjects factor and group (training, control) as between subjects factor revealed no significant main effect of time for ACS, $F(1, 24) = 2.41$, $p = .13$; PSWQ, $F < 1$, *NS*; STAI-TA, $F(1, 24) = 1.56$, $p = .22$. Furthermore, no group X time interactions were observed for any of these scales ($F < 1$, *NS* for all scales). There were no group differences for ACS, PSWQ and STAI either at the pre-intervention or at the post-intervention (all *ts* < 1, *NS*, see Table 1 for descriptive statistics.). Separate paired t-tests for each group revealed no significant difference pre to post intervention for the control group in any of these scales either (PSWQ, ACS, $t < 1$, *NS*; STAI-TA, $t(12) = 1.12$, $p = 29$). The training group also did not show any significant improvement on scores on the PSWQ and STAI (*ts* < 1, *NS*), but there was a significant trend for an increase in attentional control post vs pre intervention, $t(12) = 1.89$, $p = .08$.

Training improvement and changes in self-reported trait anxiety

Following previous recommendations on the role of training engagement in reducing negative symptomatology (see Siegle et al., 2014), we also considered how engagement with and improvement on the training task was associated with changes in self-reported trait anxiety. Here, the level of training-related improvement (i.e., mean level of difficulty in the first three days of training to the last three days) was taken as an index of the level of engagement. Based on this index, we divided the training group into two (high-engaged group, $N = 7$, $M = 1.12$, $SD = 0.33$; low-engaged group, $N = 6$, $M = 0.07$, $SD = 0.37$) by a median split and conducted an ANOVA

with change in trait anxiety (pre-intervention – post-intervention) as a dependent variable and engagement level as a between subjects factor. There was a significant effect of task engagement on change in trait anxiety, $F(1, 11) = 14.01$, $p < .01$. The high-engaged group showed a greater decrease (*Mdifference* = 4.86, *SD* = 3.29) in trait anxiety scores as compared to the low-engaged group (*Mdifference* = -3.33, *SD* = 4.59) who showed a slight increase in trait anxiety scores. In line with these results, we considered the full variation in level of engagement and trait anxiety and performed a correlational analysis between the level of engagement and change in self-reported trait anxiety (see Figure 6). Level of engagement with the training task was positively correlated with greater reductions in self-reported trait anxiety pre to post intervention in the training group, $r(13) = .59$, $p < .05$.

Discussion

The current study set out to examine whether extensive working memory training can improve attentional control processes in high trait anxious individuals. We used resting state EEG measures as an indirect neural index of trait attentional control, the flanker task as a behavioral measure of distractor interference with and without threat, and the antisaccade task with emotional faces as a measure of valence-specific inhibitory control. The causal roles of attentional control and working memory capacity as determinants of emotional vulnerability and resilience are becoming increasingly important in both theoretical models of anxiety and depression (see Berggren, & Derakshan, 2013; Waugh, & Koster, 2014) and in explaining exaggerated processing styles for negative information as well as clinical applications of such models in reducing ruminative styles of thinking (e.g., Cohen et al., 2015; Siegle et al., 2014).

Given recent theoretical debates on the usefulness of working memory training (e.g., Shipstead et al., 2012), it is of crucial importance to examine cognitive transfer of training-related

gains onto untrained tasks using multiple outcome measures. In this proof-of-principle study, we examined whether adaptive training vs. an active control training resulted in improved attentional control on behavioral as well as neural levels in various transfer tasks. Moreover, we were interested to see if training could lead to reductions in self-reported anxious symptomatology. The main results are that working memory training resulted in improved attentional control at the behavioral level assessed via the Flanker task and neural level observed in terms of SW/FW. Furthermore, level of training-related improvement was associated with reductions in levels of trait anxiety. We discuss the implications of these findings below.

Training related gains at the behavioral level were examined via the Flanker task that included a stress-related manipulation in order to assess distractor interference and cognitive control under conditions of high anxiety and competing task demands. Moreover, we examined transfer to emotional information processing on the Antisaccade task that included angry and neutral facial expressions as targets. At post intervention participants in both training and control groups showed improvements on the Flanker task in terms of their ability to resist distracting interference when identifying targets with this effect being greater in flanker blocks where state anxiety was manipulated via bursts of white noise. Crucially, when exposed to unpredictable bursts of white noise, participants in the training group showed an improvement compared with baseline whereas those assigned to the control group showed no significant improvement but rather a cost under these conditions. These results suggest that working memory training helped enhance cognitive performance under stressful situations when the efficient exercise of attentional control was required to cope with the (likely) presentation of an external aversive stimulus and enforce focusing on the (Flanker) task at hand. This interpretation dovetails with the results of the study by Otto, Raio, Chiang, Phelps and Daw (2013) that showed that during a

learning task participants high in working memory capacity did not suffer from the detrimental effects of stress as compared to the participants low in working memory capacity that did so.

Training-related gains seemed not to transfer to performance on the antisaccade task as assessed by antisaccade latencies and error rates. A closer examination of neural activity right before the onset of saccades during the 50 ms interval prior to target presentation showed no significant increase of central negativity for the training group, with the control group showing an increment only for neutral facial expressions during antisaccade trials. However, this increment on central negativity was not reflected on behavioral task performance. Hence, increased central negativity without any behavioral improvement may in fact reflect the inefficient use of cognitive resources towards achieving behavioral outcomes (see Ansari & Derakshan, 2011a,b) suggestive of the fact that in the absence of anxiety-related difference in terms of antisaccade latencies increased cognitive effort without any advantage on performance may reflect deficiencies in processing efficiency towards the desired behavioral outcome. Nevertheless, results with regard to antisaccade performance were not in the expected direction.

One plausible explanation for the lack of a significant transfer effect could be related to the use of emotional targets in the antisaccade task which may have necessitated some form of emotional working memory training or control (see Schweizer, Hampshire, & Dalgleish, 2011) facilitating the specific processes underlying selective attention to and inhibition of threat-related material. Accordingly, future studies should investigate the transfer of training related gains on an Antisaccade task that incorporates neutral shaped objects (e.g., oval shapes e.g., Derakshan, Saville & Course-Choi, in preparation) rather than emotional faces. It is worth mentioning that the working memory training transfer effects in Owens et al (2013) were also observed in relation to enhanced inhibitory control and the filtering of irrelevant information devoid of emotional content. Furthermore, the antisaccade task used in the current study followed a blocked design

(separate blocks for antisaccade and prosaccade trials). Future research can examine training related effects on a more challenging version of a mixed antisaccade task where anti and prosaccade trials are mixed (Ansari, Derakshan, & Richards, 2008; Vanlessen, De Raedt, Mueller, Rossi, & Pourtois, in press).

Finally, working memory training resulted in transfer of gains to resting state EEG, as measured by SW/FW ratio. The ratio between the power density in SW and FW band frequencies has been previously related to trait attentional control (Putman et al., 2014). While increased SW/FW is related to attentional problems (Clarke et al., 2001; Arns et al., 2011), decreased SW/FW is related to better attentional control (Putman et al., 2012, 2014). In our study, we observed a reduced SW/FW for the training group only. Although improvement on a trait-like measure in a short time period (3 weeks) is remarkable, trait-like improvements like fluid intelligence (Au et al., 2014; Schweizer et al., 2011) or WM capacity (Schweizer et al., 2013; Owens et al., 2011) were observed as a function of WM training in many other studies as well. This finding is valuable as it may indicate that working memory training can yield improvements in attentional control mechanisms at the neurophysiological level.

Training Related Gains on Anxiety Vulnerability, and Clinical Implications

An interesting finding concerns the relationship between training-related improvements and changes in self-reported anxiety which was amongst our primary goals. Although we did not observe any group differences on anxiety scores at post-intervention, we found decreased anxiety scores for participants who improved the most on the training task. While high-engaged participants showed decreases in levels of trait anxiety, low-engaged participants showed the opposite pattern. The relationship between training improvement and decreased anxiety was also evident at a correlational level indicating that increased engagement was related to decreased

anxiety scores. This finding is valuable as it may indicate that the higher engagement with the task, the greater processing efficiency and reductions in anxious symptomatology. From a motivational perspective, this finding extends previous claims that higher levels of motivation could predict greater engagement with the task, which might in turn be related to enhanced training related gains (Jaeggi, Buschkuehl, Shah, & Jonides, 2014). Furthermore, this finding resembles effects obtained in clinical depression (Siegle et al., 2014) where applied cognitive training in a depressed population undergoing psychotherapy and medication led to additional benefits in treatment outcome for participants who engaged with the task to a greater level. Due to the limitations considered with our small sample sizes in each group replication with a larger sample to examine the relationship between training related gains and anxiety would be highly desirable.

Conclusions, Limitations and Future Directions

In line with the ACT (Eysenck et al., 2007), we observed that improved levels of working memory performance was related to improved attentional control, especially when participants were required to perform the flanker task under stress, as well as to reductions in self-reported anxious symptomatology post relative to pre intervention, and resting state neurophysiological indices of attentional control. Such improvements were observed under conditions where anxiety elicited effects could be maximally observed (Berggren, Koster, & Derakshan, 2012; Berggren & Derakshan, 2013). It can be argued that working memory training led to increases in the regulation of top-down control mechanisms, thereby resulting in decreased interference from bottom-up influences in trait vulnerability to anxiety. Despite such improvements in performance and resting state EEG, the transfer effects on inhibitory control as assessed by the antisaccade task were less conclusive and future research should examine the possible transfer effects of

adaptive cognitive training using the dual n-back on non-emotional versions of the antisaccade task (e.g., Derakshan et al., in preparation). While the current study elucidates the link between attentional control and anxiety within the ACT framework, and sheds some light on the mechanisms in working memory responsible for the effects of anxiety on performance, it opens up fruitful avenues for future work to explore further the exact processes that need targeting in training paradigms. Here, working memory was trained and training related gains on attentional control was assessed in a broad fashion. Currently, the state of the literature on training does not specify whether distinct components of attention are trained. If working memory training influences attentional control in a broad sense one would expect changes across a range of different attentional tasks. However, provided that training related transfer was not observed on every attention task in the current study this begs the question how each of the specific attentional processes (e.g., either inhibition, shifting or updating information) might be influenced as a function of working memory training. Moreover, whether these effects then generalize to other processes of working memory remains an open question (see Shipstead et al., 2012).

It will be beneficial for future studies to consider having follow-up sessions of testing to examine the stability of the obtained transfer effects. Although extensive working memory training studies are resource extensive, future research should have a greater number of participants in each group. Our sample sizes in the current investigation were small, which made it difficult to eliminate the effects of individual differences at group level and might be responsible for some of the baseline differences between the training and control group, for example on antisaccade latencies. Although, these differences were statistically controlled, with a greater sample size more solid conclusions can be reached.

In conclusion, this study contributes to our understanding of the causal relationship between attentional control mechanisms and anxiety. Our findings suggest that working memory training may have a beneficial contribution to improve attention or inhibition-control deficits typically associated with anxiety, and the vulnerability to develop anxiety disorders. The results of the current investigation pave the way for more extensive and multilevel investigations of how working memory training through its influence on attentional control may help protect against trait vulnerability to anxiety.

Acknowledgements

The research was funded by the Fund for Scientific Research-Flanders (FWO, #G094012N) awarded to E.K., G.P., & N.D. We would like to express our thanks to Inês Mares and Nick Berggren for their help with the data collection.

Footnotes

[1]There was a marginal group difference at pre-test for the control group for the noise block, $t(21) = 1.74$, $p = .10$, but for the safe block, $t(21) = 1.26$, $p = .22$. There was no group difference at the post-test for the noise block, $t < 1$, *NS* and a marginal difference for the safe block, $t(21) = 1.77$, $p = .09$.

[2]In keeping with Ansari and Derakshan (2011a) and Everling et al. (2001), we also looked at the frontal negativity (averaged F3, F4, Fz). However, due to technical problems these channels were considerably noisy as compared to central ones and did not lead to any significant group X time X valence interactions, $F < 1$, *NS* (for antisaccade); $F(1, 23) = 1.06$, $p = .31$ (for prosaccade).

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Figure Captions

Figure 1. The flow of *n*-back task. An example of a 2-back trial.

Figure 2. Performance of the training group over time on dual n back task.

Figure 3. Gains in attentional control (reductions in SW/FW ratio) for control and training group separately.

Figure 4. Gains in interference reduction for Flanker task for noise and safe blocks in control and training groups.

Figure 5a. Central Negativity for pre to post-intervention (positive value indicates increased negativity) for the control group for neutral and angry trials. Negative is plotted down. Waveforms were filtered with a high cutoff filter of 5 Hz (slope 24 dB/oct) for visual inspection.

Figure 5b. Central Negativity for pre to post-intervention (positive value indicates increased negativity) for the training group for neutral and angry trials. Negative is plotted down. Waveforms were filtered with a high cutoff filter of 5 Hz (slope 24 dB/oct) for visual inspection.

Figure 6. The relationship between training improvement/level of engagement (averaged performance on last 3 days – first 3 days) and reduction in trait anxiety scores.

Figure 1

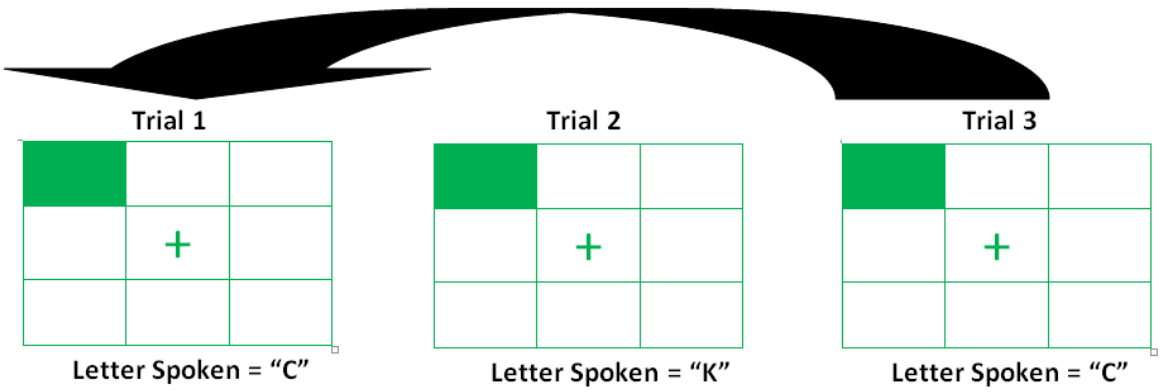


Figure 2

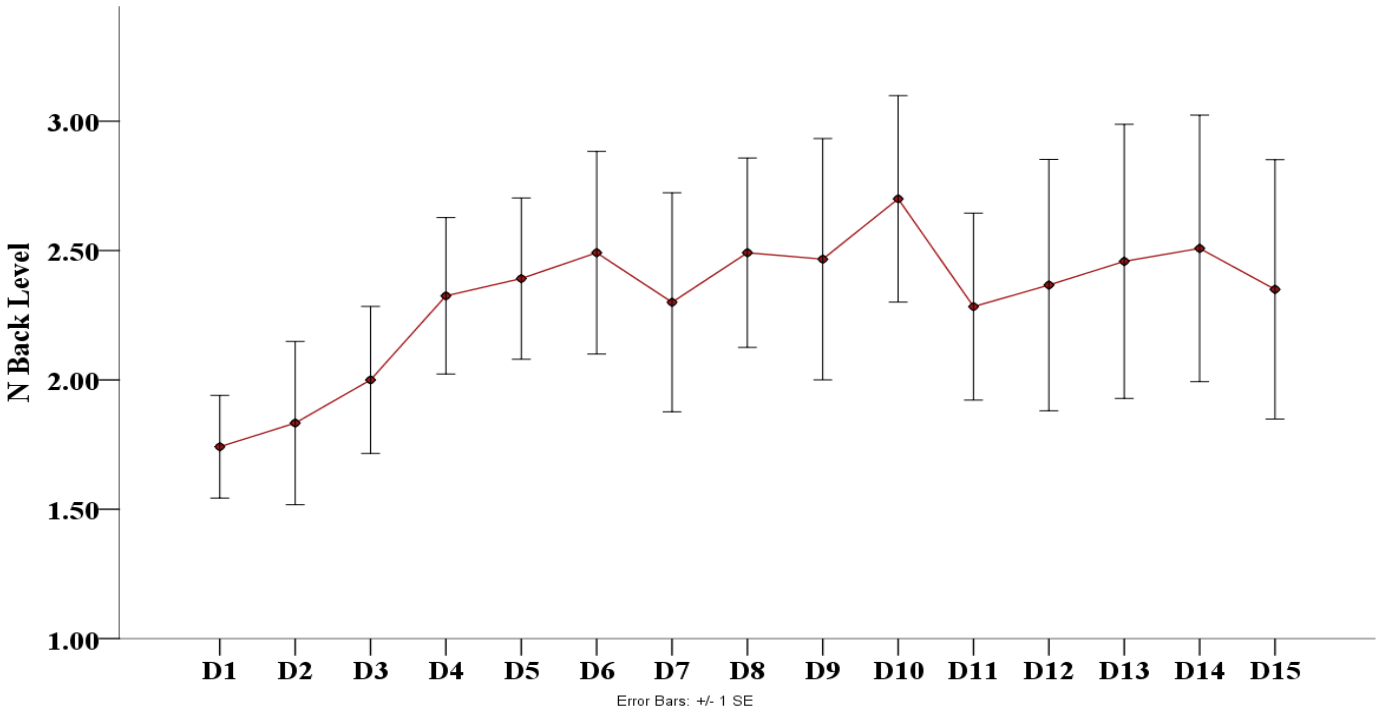


Figure 3

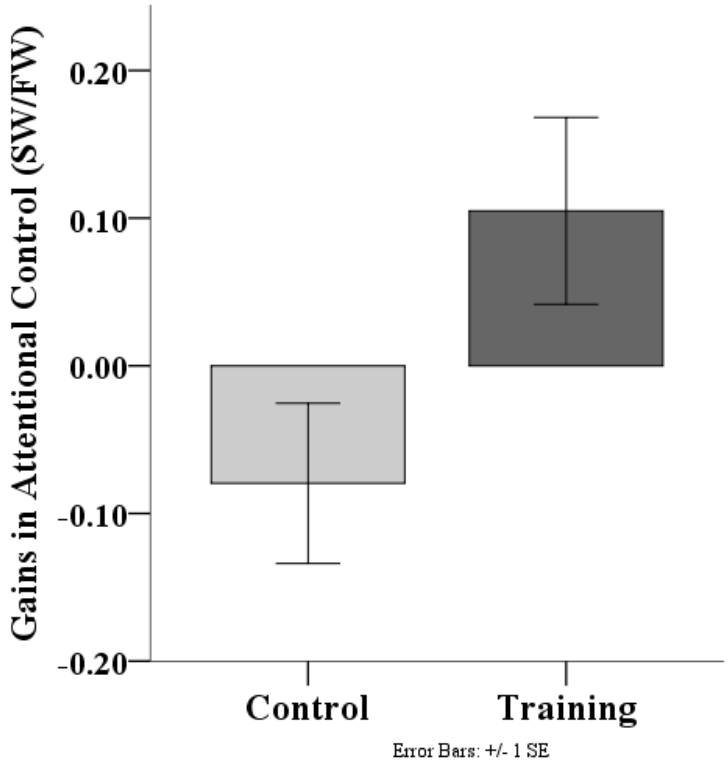


Figure 4

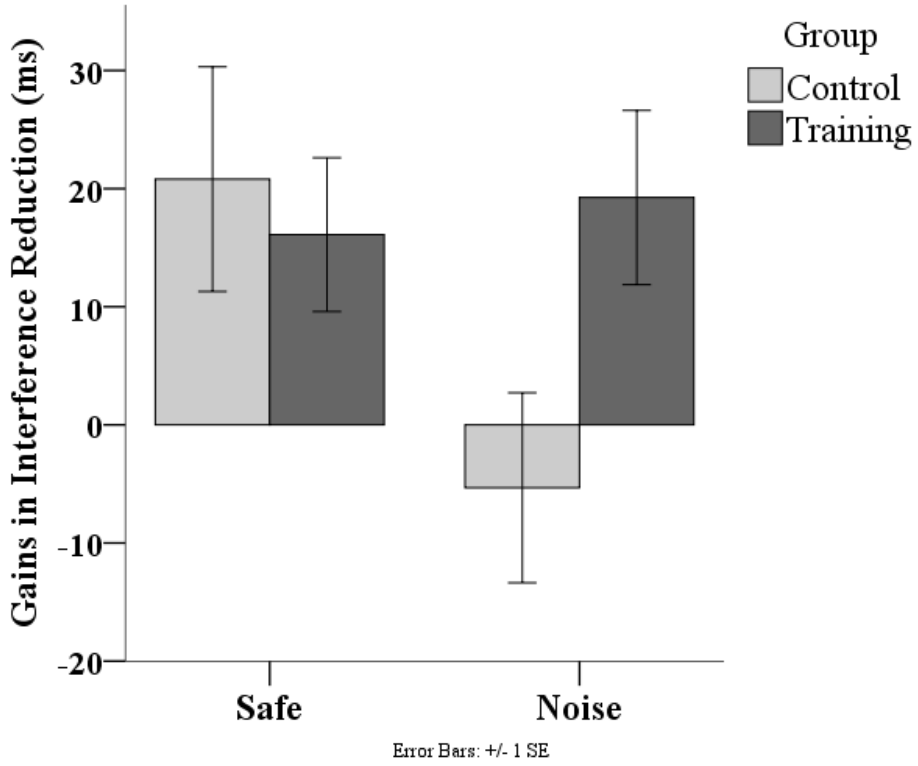
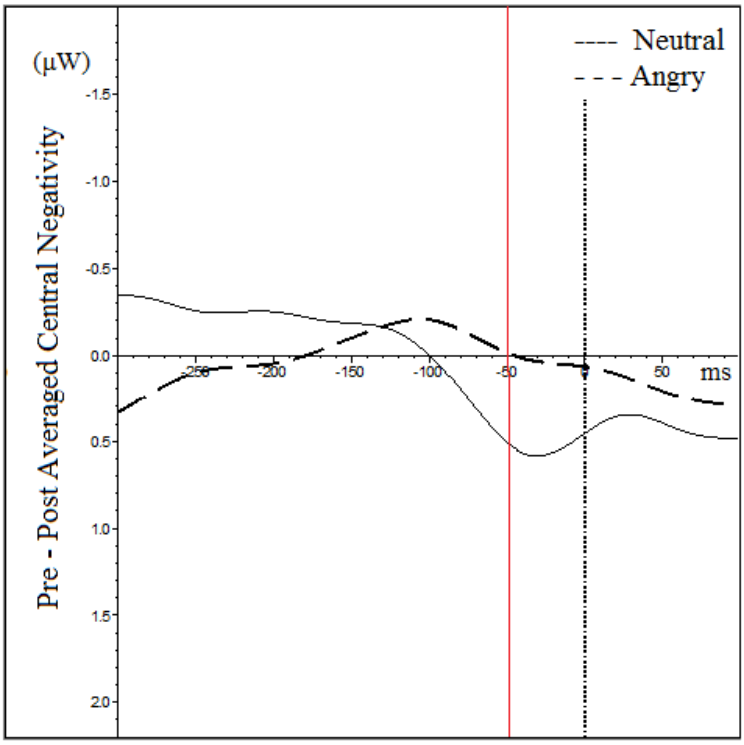


Figure 5a – 5b



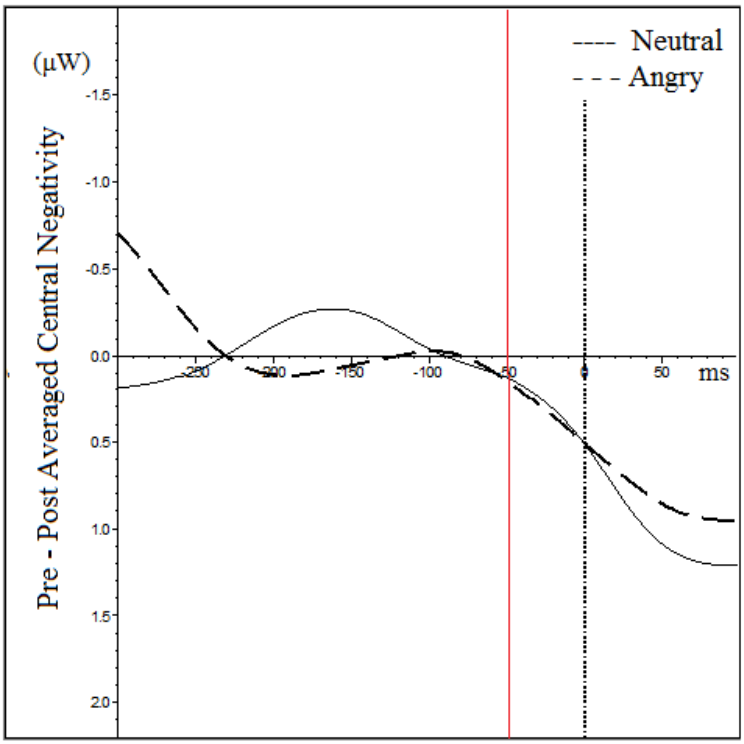
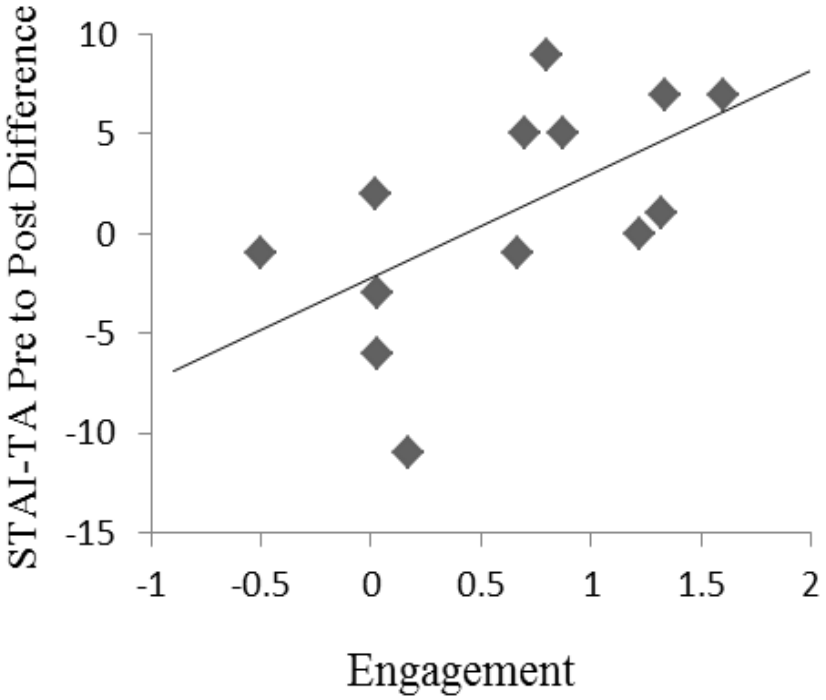


Figure 6



Table

Table 1. Mean self-reported symptomatology at pre- and post-intervention for control and training group separately (*SD*s are presented in parentheses).

	Pre-intervention		Post-intervention	
	Control	Training	Control	Training
ACS	45 (12)	44 (8)	46 (10)	45 (9)
PSWQ	64 (12)	66 (7)	62 (11)	65 (9)
STAI-TA	57 (8)	56 (9)	55 (9)	55 (9)