Adaptive working memory training can reduce anxiety and depression vulnerability in adolescents

Patricia Beloe and Nazanin Derakshan

Department of Psychological Sciences, Birkbeck University of London, UK

Corresponding address:

Ms Patricia Beloe

Department of Psychological Sciences

Birkbeck University of London

London UK.

Email: pbeloe01@mail.bbk.ac.uk

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Research Highlights

- Adaptive working memory training can reduce sub-clinical anxiety and depression-related symptomatology in adolescents, with the effects of adaptive training sustainable at 1-month follow-up.
- This is the first time that adaptive *n*-back training has been shown to impact depression symptoms.
- We highlight challenges facing research on cognitive training interventions for adolescents.

Abstract

Adolescents can be at heightened risk for anxiety and depression, with accumulating research reporting on associations between anxiety and depression and cognitive impairments, implicating working memory and attentional control deficits. Several studies now point to the promise of adaptive working memory training to increase attentional control in depressed and anxious participants and reduce anxiety and depression symptoms, but this has not been explored in a non-clinical adolescent population.

The current study explored the effects of adaptive dual *n*-back working memory training on sub-clinical anxiety and depression symptomology in adolescents. Participants trained on either an online adaptive working memory task or non-adaptive control task for up to 20 days. Primary outcome measures were self-reported anxiety and depression symptomology, before and after intervention, and at 1-month follow-up. Self-reported depression ($p = .003$) and anxiety ($p = .04$) decreased after training in the adaptive *n*-back group relative to the non-adaptive control group in the intention-to-treat sample ($n = 120$). These effects were sustained at follow-up. Our findings constitute proof of principle evidence that working memory training may help reduce anxiety and depression vulnerability in a non-clinical adolescent population. We discuss the findings' implications for reducing risk of internalising disorders in youth and the need for replication.

Keywords: Attentional Control, Anxiety, Adolescents, Working Memory Training

1. Introduction

1.1. Background

Anxiety is one of the most common mental health disorders in youth (Beesdo, Knappe & Pine, 2009). Despite recurrent anxiety symptoms in childhood, clinically significant anxiety often does not emerge until adolescence, when reported anxiety-related problems peak (Gagne et al., 2017; Shirtcliff, Zahn-Waxler & Marceau, 2007). Furthermore, anxiety disorders in early adolescence represent a risk for developing subsequent depression (Bittner et al., 2004; Davies et al., 2016; Meier et al., 2015). There are growing societal concerns about increasing prevalence of such disorders in children and young people (Calling et al., 2017; Mojtabai, Olfson, & Han, 2016; Twenge, Joiner, Rogers & Martin, 2018), however the reasons for increased prevalence remain unclear (Collishaw, 2014; Twenge et al., 2018).

Cumulative research points to the instrumental role of attentional control in vulnerability to anxiety and depression (Berggren & Derakshan, 2013; Koster et al., 2017), where attentional control refers to individual differences in the ability to regulate attention, awareness and concentration (Helzer, Connor-Smith & Reid, 2009; Rothbart & Bates, 2006). Several studies find evidence of associations between variation in the capacity to exercise voluntary control over mental resources and anxiety and depression in both children and adolescents (Kertz, Belden, Tillman & Luby, 2016; Sportel et al., 2011). There is also evidence of a shared genetic etiology for attentional control and anxiety, such that poorer attentional control may represent a phenotypic and genetic risk factor for anxiety disorders during adolescence (Gagne et al., 2017).

Attentional Control Theory (ACT: Eysenck et al., 2007) provides a productive theoretical framework for exploring links between attentional control and internalizing. ACT proposes that anxiety increases the influence of bottom-up over top-down attentional processes. Anxiety-related cognitions and worry exhaust attentional control resources, influencing critical executive functions and increasing demand for compensatory cognitive resources to make up for the effects of poor attentional control (Berggren & Derakshan, 2013). Effects may be similar for rumination, the pattern of repetitive negative thinking about the past, which is characteristic and predictive of depression in adults (Nolen-Hoeksema, 2000). Reduced ability to intentionally direct attention away from worrisome thoughts or persistent negative self-talk may explain how worry and rumination increase vulnerability to anxiety and depression (Koster et al., 2017).

Attentional control is a core component of working memory (WM), instrumental for goal-directed maintenance and manipulation of information in WM (Shipstead, Lindsey, Marshall & Engle, 2014). The role of attentional control and WM as determinants of vulnerability and resilience in emotional disorders is highlighted in recent reviews (Koster et al., 2017; Moran, 2016). Extant research tends to focus predominantly on adults, but there is also evidence that childhood WM performance predicts subsequent adolescent psychopathology (Rinsky & Hinshaw, 2011) and that WM may modulate the association between anxiety and cognitive performance in adolescents (Owens, Stevenson, Norgate & Hadwin, 2008) and children (Hadwin, Brogan & Stevenson, 2005;–Visu-Petra, Cheie & Miu, 2013). Anxiety may also disrupt verbal WM (Visu-Petra et al., 2013), consistent with the adult literature, and may reflect the verbal nature of worry and rumination (Onraedt & Koster, 2014; Vytal et al., 2013).

Adolesence marks a period of significant developmental change and maturation in the neural networks associated with attention control and working memory (Crone et al., 2006, Giedd et al., 1999, Nagy, Westerberg & Klingberg, 2004, Raznahan et al., 2011) and such cognitive processes may be under particular strain during this developmental period. Some researchers suggest vulnerability to mental illness in teenagers is linked to rapid changes in brain structure and function (Paus, Keshavan & Giedd, 2008). Therefore, typically developing children and young people with emotional vulnerability may benefit from bolstering of these resources to reduce the risk of emotional disorders and we propose that training attentional control via working memory may be a viable way of doing so.

A growing literature has been investigating if cognitive improvements via working memory can transfer to improvements in academic performance or performance on tasks relying on executive functions supported by attentional control. The results of several contradictory meta-analyses mean there is no consensus that cognitive training improves performance on any measures beyond those practiced in training protocols themselves (see Au et al., 2015; Au, Buschkuehl, Duncan & Jaeggi, 2016; Melby-Lervåg, Redick & Hulme, 2016; Shipstead, Redick & Engle, 2012). However, this absence of consensus on transfer to academic measures does not preclude transfer to affective processes.

Accumulative evidence shows promising effects for attentional control training via WM on internalising symptomology (reviewed in Koster et al., 2017; Motter et al., 2016). Research amongst adolescents is relatively scant however. In two studies, Hadwin and Richards (2016) and Roughan and Hadwin (2011) found reduced anxiety and emotional and behavioural difficulties following WM training. Neither study featured robust controls and sample size was limited in one case. However, in a recent well-controlled study, Schweizer et al. (2017) found emotional WM training led to significant reductions in post-traumatic stress disorder symptoms (PTSD) in adolescents awaiting treatment for PTSD.

It is apt therefore to explore the potential of WM training as a preventative intervention aiming to reduce risk for developing internalising disorders during adolescence. No studies have investigated its effects on anxiety and depression symptoms in a typically developing non-clinical adolescent population, and the goal of the present study was to examine if WM training might impact self-reported anxiety and depression symptomology in such a developmental group.

1.2. The current study

We employed an adaptive dual *n*-back task similar to that used by Sari et al. (2016) and Swainston & Derakshan (2018). WM training induces cognitive plasticity when the cognitive system is induced to perform above its routine functioning by new external demands (Lövden et al., 2010; Von Bastian & Eschen, 2016). This 'stretching' of the system must be facilitated by an appropriate training task, whilst maintaining the demands on the system within a 'Goldilocks zone' of 'just enough' challenge. The principle of an adaptive *n*-back training task is that its difficulty increases commensurate with the individual participant's proficiency. By making gradual cumulative demands on WM, increasingly higher performance levels are attained and working memory capacity may be increased (Klingberg, 2010; Von Bastian & Eschen, 2016).

A variety of working memory and attentional control training tasks have been used to target affective processes (see Koster et al., 2017). One research group found evidence that WM training tasks may require an emotional dimension to be clinically effective (Schweizer, Hampshire & Dalgleish, 2011), however the outcome measures in this study related to emotional regulation/affective control processes rather than psychopathology measures. Schweizer et al. (2017) found PTSD amelioration following emotional *n*-back training, however it was not compared with a neutral training task. In general however, other groups have found cognitive training led to reduced psychopathology symptoms with neutral task stimuli (see Koster et al., 2017). There is evidence that the adaptive dual *n*-back task used in our study is an effective training task for increasing working memory capacity (Jaeggi, Buschkuehl, Jonides & Perrig, 2008) and has already shown promise as a training intervention to target anxiety and depression vulnerability. Training using this paradigm has previously led to improvements in inhibition, WM capacity and cognitive control that were associated with reduced anxiety and depression-related symptomatology (Course-Choi, Saville & Derakshan, 2017; Grol et al., 2018; Sari et al., 2016; Swainston & Derakhsan, 2018).

Typically, active controls are necessary to avoid Hawthorne effects in intervention studies (McCambridge, Witton & Elbourne, 2014). In this study the intervention group was compared with an active control group which trained on a non-adaptive version of the task. In the non-adaptive control task, challenge remains at the beginner level. Thus, the demand on WM over the training period never changes and neural plasticity is not induced (Klingberg, 2010). Such a control is widely used in WM training studies (see Holmes, Gathercole & Dunning, 2009; Karbach, Strobach & Schubert, 2015; Klingberg, 2010). An additional rationale for a non-adaptive version of the task is that where study participants are from cohort of young people from the same school and likely to compare notes, it is crucial the control training appears equivalent to the active intervention, as much as is possible. Many adolescents are well educated on the scientific method, so using the non-adaptive control task should mean participants were less likely to deduce a hypothesis and that they were in a control group.

Training transfer was assessed using the Revised Child Anxiety and Depression Scale (RCADS: Chorpita et al., 2000) which features two composite measures (one for total anxiety and another for anxiety combined with depression), plus several subscales assessing different categories of anxiety and depression. We predicted that adaptive training would lead to significant reductions in scores on the RCADS scales directly following intervention with sustained effects at 1-month follow up.

2. Method

2.1. Participants

Participants were pupils from two independent single-sex secondary schools in southeast England. After an information evening and letter of invitation to parents and students, 254 pupils volunteered [141 boys (mean age = 12.8) and 113 girls (mean age =13.06)]. The mean age overall was 13.08 (SD = 1.7) and ranged from 10-18 years. Written informed parental and participant consent was obtained. Participants were assigned to the *n*-back training or active control groups via a system of sequentially alternating allocation to either condition (*n*-back; n = 128, 58 = female: control; n = 126, 55 = female). Participants, parents, and the school staff involved in participant recruitment and adherence were all blind to group allocation. Ethical approval was granted by the research ethics committee of the Department of Psychological Sciences at Birkbeck University of London.

2.2. Materials and experimental tasks

Primary outcome measure: Participants completed the Revised Child Anxiety and Depression Scale (RCADS, Chorpita et al., 2000), a questionnaire validated for assessing self-reported anxiety and depression in 10-16 year olds. Its 47 items relate to six discrete subscales; Generalised Anxiety Disorder, Panic Disorder, Obsessive Compulsive Disorder, Separation Anxiety, Social Phobia and Depression. Answers to items are rated on a 4-point Likert scale, ranging from 0 (“never”) to 3 (“always”). It yields scores for each subscale, plus two composite scores - Total Anxiety (sum of the 5 anxiety subscales) and Total Internalising (sum of 5 anxiety plus 1 depression subscales – 6 in total). The subscales and composite scales are considered to have good reliability (Chorpita, Moffit & Gray, 2005) and test-retest reliability at one week (Chorpita et al., 2000). There is evidence of good concurrent reliability with the Children’s Depression Inventory and the Revised Children’s Manifest Anxiety Scale (Chorpita et al., 2005). Although not previously validated in a typically developing UK sample, the RCADS has been reported as a reliable and valid instrument for measuring internalising symptoms in the general population and school samples in Australia, the Netherlands, Denmark and the US, and in clinical and school samples in Hawaii (Koesters et al., 2015).

Of interest in the current study were scores on the two composite measures (Total Anxiety, Total Internalising) plus the Depression subscale, allowing us to capture overall anxiety and depression symptomology.

Reading outcome

Data was also collected on the effects of *n*-back versus non-adaptive control training on reading outcomes using a standardised measure, the New Group Reading Test (NGRT) (GL Assessment, 2013).[1]

2.3. Working memory training

Adaptive dual *n*-back training task: This task was equivalent to that used by Sari et al., (2016). Each training trial features a 3 X 3 grid with nine white spaces, starting with a fixation cross at a central point on the screen. A green block appears in one of the 9 spaces, accompanied by a female voice announcing a letter (L, A etc.). Participants must remember the location of the green square and the letter's identity. This is followed by another trial stimulus. The location of the green block and the announced letter may be the same or different from the previous trial. Depending on the difficulty level, the participant indicates whether the current trial matches the one immediately before, or two, three or even four trials back. Hence *n*-back; '*n'* referring to the number of trials earlier with which the current trial is compared. If locations match, participants press 'A' on the keyboard and press 'L' if the letter matches. Participants press both keys if location and letter sound match the comparison trial. If there is no match, no key is pressed.

Participants begin at the 1-back level. When 95% accuracy is attained in a block, the participant moves to the 2-back level, where stimuli are compared with trials two steps previously, and so forth. If 75-95% accuracy is not sustained at a new level, they return to the previous level in the following block. The task is adaptive because *n*-level increases or decreases

[1] This is not discussed further here as there were no effects of training on standardised reading. Results of the analysis may be found in the supplementary materials.

in response to performance. Each training session consists of 20 blocks, with each block lasting 30 minutes. Each block features 20 trials. There is a 20-second pause between blocks with a countdown to the start of the next block. The upcoming *n*-back level is always indicated following this pause and before trials begin.

Active control task: : This task is a non-adaptive version of the dual *n*-back training where difficulty stays at 1-back; participants only compare target trials with the immediately preceding trial.

2.4. Procedure

Participants were instructed (in groups of 30) on the training tasks and questionnaires during half-hour training sessions and afterwards assigned to either the adaptive *n*-back or control intervention. Participants were told that we were testing different versions of the training, but not informed that there was a control. Participants were informed about study hypotheses in a debrief at the end of the study and all control participants were invited to do the adaptive training.

The computerized training intervention was performed online daily using personal or school computers. Each participant had a unique URL to access the training and questionnaires. On logging in for the first time, participants completed the RCADS self-report questionnaire (time 1). During the first session, participants performed as many practice blocks as desired before commencing the training blocks. Training took place over a period of 4 weeks to permit participants to complete 5 days' training per week, with 2 days off, yielding a maximum of 20 days' training. This is roughly consistent with many previous WM training interventions providing opportunities to train for up to 25 days (e.g. Holmes, Gathercole & Dunning, 2009;

Klingberg, 2010). This time frame was also chosen to allow the study to be accommodated within the participating schools' schedule. Participants were therefore instructed to practice the task at least 5 days per week over a period of 4 weeks, at roughly the same time each day in a quiet space with no distractions. Participants could view performance data after the final block. Only one session per day was permitted, with all blocks completed in one attempt. After four-weeks (time 2), and at one-month follow-up (time 3), participants completed the online RCADS questionnaire.

Participants received a daily training prompt via email. Adherence was monitored by the researcher and missed sessions were communicated to school staff every other day. If training was missed, participants received a personal email of encouragement from the school. Reminders ceased after seven consecutive days where no training took place. This procedure was consistent across both schools, although the wording of emails was at the discretion of school staff.

2.5. Statistical methods

Data were analysed using IBM SPSS Statistics, Version 22.0. 2 (Group: *n*-back, control) X 3 (Time: time 1, time 2, time 3) Linear Mixed Effect Models (MLMs) compared groups on RCADS anxiety and depression measures across time. Fixed effects were specified for Group (*n*-back, control), Time (time 1, time 2, time 3), and a Group x Time interaction. Data were analysed according to an intention-to-treat (ITT) principle whereby the initial sample with adequate training dosage (n = 120, *n*-back = 59; control = 61) were analyzed, regardless of whether participants completed anxiety and depression scales across the entire intervention. Model estimation was with the maximum likelihood method. Cohen's d effect sizes were derived from the F test ($d = 2*\sqrt{(F / df}$). In addition, a MLM was applied to the per protocol (PP) sample which included only the participants for whom there was anxiety and depression data at all three time points (*n*-back, n = 27; control, n = 30).

3. Results

3.1. Training adherence and data analysis approach.

Figure 1 summarizes the flow of participants through the study. Of the 254 pupils who volunteered, 87 (*n*-back n = 45; control n = 42) withdrew/completed no training. The remaining participants (n = 167) did not complete equal amounts of training, with adherence varying from 1-20 days. Figure 6 shows the distribution of training across participants. The mean number of days trained was 10.81 days (SD = 6.36) and the mode was 20 days. Some research indicates *n*-back training effects may emerge around 8 days (Jaeggi et al., 2008), while Peng and Miller's

(2016) meta-analysis concluded attention training duration does not significantly influence training effects. This evidence combined with the fact that in the present study steepest improvements in *n*-back performance occurred in the first 5 days of training (see figure 2), led us to consider ≥ 6 days' training as likely adequate dosage for analysis, resulting in n=120 participants with sufficient training.

Insert Figure 1 here

Insert Figure 6 here

The ITT group (n = 120) ranged in age from 10 to 18 years with a mean of 13 years (*SD* = 1.58 [*n*- back], 1.71 [control]). Mean training dosage in the n- back training group was 13.31 days (SD = 4.95) and amongst the active controls was 14.13 days (*SD* = 5.1). The groups did not differ on training dosage $t(118) < 1$, *NS*. Age significantly predicted number of days' training $\beta = -0.809$, $t(119) = 22.97$, $p = 0.004$, and explained a small but significant proportion of training adherence $R = 0.07$, $F(1, 119) = 8.82$, $p = 0.004$. The gender of participants did not differ between the control and adaptive training group (n- back, 27 males, 32 females; control, 28 males, 33 females) χ (1) < 1, NS, n = 120). Groups did not differ in age (*n*- back, *M* = 13.2, *SD* = 1.58; control, *M* = 13.1, *SD* = 1.71), $t(118) < 1$, NS.

Amongst these participants n = 57 completed the psychopathology questionnaires 3 times. Per protocol (PP) sample analysis was conducted on this group. There were no significant gender differences between groups (*n*-back; male = 11, female = 16: control; male = 6, female = 24) $\chi2$ (1) = 2.92, p = .09 (n = 57). The mean number of training days for RCADS completers was *M* = 14.86, *SD* = 4.77 and the groups did not differ on number of days' training exposure (*n*-back *M* = 14.63, *SD* = 4.85; control *M* = 15.07, *SD* = 4.76), $t(55) < 1$, *NS*.

47 participants completed 1-5 days training only, with similar numbers in each group (*n*-back n = 24, control n = 23). The average age was 12.96 years (SD = 1.93). For this group of very poor adherers, the mean training dose was 3.36 days (*SD* = 1.30). The distribution of training adherence was bimodal with 3 (n = 15) or 5 (n = 12) days the most common dose. Within this group only n = 15 responded to the questionnaire at all three time points, while n = 5 did not respond to the questionnaires at all. Amongst the remaining poor adhereres, n = 15 responded at Time 1 (T1) only, n = 7 completed T1 and Time 2 (T2) only, whilst n= 5 participants responded at T1 and Time 3 (T3) only.

3.2. Sensitivity analysis

To address variable training exposure a sensitivity analysis explored the relationship between training dosage and change in self-reported psychopathology from pre-intervention (T1) to both post intervention (T2) and follow-up (T3). There was no significant association between the number of training days and changes in symptomology, comparing T1 with T2 or T3 for Total Anxiety (all rs < -.03, ps > .8) Total Internalising (all rs < .04, all ps > .7) and Depression (all rs < .16, all ps > .27). We conducted an identical analysis with the poor adherence group (≤5 training sessions) and all t's <1, *NS*.

3.3. Dual n-back working memory training performance

N-back training - Figure 2 illustrates mean *n*-back achieved by ITT group participants (n = 120) across the training period. WM performance improved significantly, evidenced by higher mean *n*-back level on the last day of training (*M* = 2.36, *SD* = 1.03) relative to the first (*M* = 1.82, *SD* = 0.48) $t(58) = 4.84$, $p < .001$.

Insert Figure 2 here

1-back active control training - Percentage accuracy in 1-back performance amongst the active control group was unchanged between the beginning (M = 93.58, SD = 9.81) and end (M = 92.43, SD = 9.02) of training, $t(60) < 1$, *NS.*

The training improvement slope for the *n*-back task was significantly negatively correlated with Total Internalising (r = -.243, p =.027, n = 83) at baseline T1).

3.4. Effects on primary outcome measures

Changes in self-reported anxiety and depression symptomology

Means and standard deviations for scores on the RCADS are presented in table 1 for both ITT and PP samples respectively. The groups were not significantly different from one another prior to intervention on any measures, all t's ≤ 1, *NS*. Standardized RCADS scores ≥70 are clinically significant, whilst scores ≥ 65 are borderline clinically significant. The means for both the *n*-back and the control groups in this study were below average. 5% of the ITT sample participants scored at borderline clinical or clinically significant levels of total anxiety, whilst 11.6% had internalising scores ≥ 65. Of these participants with borderline or clinical significant anxiety, the average training days was 9.27 (SD = 1.64) with one of these participants completing fewer than 5 training days.

Total Anxiety symptomatology

Figure 3 shows that relative to the controls there was a decrease in RCADS Total Anxiety scores in the *n*-back training group, which was sustained at follow-up. The MLM for the ITT sample confirmed this observation with a significant Group X Time interaction $F(2, 98.33) = 3.42$, $p = .04$, Cohen's $d = .37$ (ITT). The MLM for the PP sample missed significance $F(2, 66.33) = 2.61$, $p = .08$, Cohen’s $d = .39$.

Age did not moderate the association between training and symptom reduction. There was no interaction effect between training days and age on Total Anxiety difference scores between T1 and T2, $F(3, 95) = .972$, *NS,* $R^{2} = .03$.

Insert Figure 3 here

Total Internalising symptomology

Figure 4 shows that relative to the controls there was a decrease in RCADS Total Internalising scores amongst participants in the *n*-back training group, which was sustained at follow-up. The MLM confirmed this observation with a significant Group X Time interaction $F(2, 89.17) = 3.86$, $p = .03$, Cohen's $d = .41$ (ITT). The MLM for the PP sample missed significance, $F(2, 67.18) = 2.64$, $p = .08$, Cohen's $d = .39$.

Insert Figure 4 here

Age did not moderate the association between training and symptom reduction. There was no interaction effect between training days and age on difference scores for Total Internalising between T1 and T2, $F(3, 95) = .674$, $NS = R^{2} =$ .02.

Depression

Figure 5 shows that relative to the controls, there was a considerable decrease in RCADS self-reported depression scores amongst participants in the *n*-back training group, which was sustained at follow-up. This observation was corroborated in the MLM by a significant Group X Time interaction $F(2, 89.65) = 6.39$, $p = .003$, Cohen's $d = .52$ (ITT); $F(2, 65.94) = 3.93$, $p = .02$, Cohen's $d = .44$ (PP).

Insert Figure 5 here

Symptom change at the individual level.

Figures S1, S2 and S3 (in supplementary materials) display individual participant symptom change from T1 to T2 with mean group change in *n*-back and control groups for Total Anxiety, Total Internalising, and Depression. In a post hoc analysis we explored the extent to which significant symptom reduction occurred at the individual level. Since our study instruments did not yield an objective measure for 'significant improvement' for an individual, we identified participants for whom difference scores were greater than the overall mean change which was -.04 across both groups. However -.04 was low benchmark. Instead we choose the mean difference in the *n*-back group as our cut off. In the ITT sample, where 46 participants from the *n*-back group completed the RCADS at T1 and T2, the mean Total Anxiety improvement was a reduction of 2.0 (SD = 5.66) and for Total Internalising a reduction of 2.3 (SD = 5.82). For both Total Anxiety and Total Internalising measures, 20 x *n*-back group participants had improvement scores that exceeded the average improvement between T1 and T2.

4. Discussion

Previous studies have shown that cognitive training may increase cognitive flexibility and reduce emotional vulnerability in clinically and sub-clinically anxious and depressed adults. The current study investigated if cognitive training using an adaptive dual *n*-back working memory task can reduce self-reported anxiety and depression symptoms in adolescence, when compared to a non-adaptive active control group. *N*-back training was significantly associated with reduced self-reported anxiety and depression symptomology relative to the controls directly following intervention and at one month follow-up. Our findings suggest that amongst adolescents it may be possible to reduce subclinical anxiety and depression symptoms using an intervention which is known to train WM (Au et al., 2016; Klingberg, 2010). Whilst WM training transfer to academic measures remains elusive, emotional processes may be more amenable to training transfer in this age group.

These findings are consistent with previous studies, which found reduced self-reported anxiety (Hadwin & Richards, 2016) and teacher-reported emotional symptomology (Roughan & Hadwin, 2011) in school children following WM training using Cogmed (Cogmed RM, Pearson), a computerized training package which targets attention and memory in academic underperformance and individuals with ADHD (Shipstead, Hicks & Engle, 2012). It is also consistent with recent adult studies which reported training-related improvement in anxiety and worry symptoms in high worriers (Course-Choi et al., 2017) and high trait anxious individuals (Sari et al., 2016). This study is however the first to find reductions in depression symptomology following adaptive dual *n*-back training. Previous studies have found that *n*-back training reduced anxiety symptoms in female breast cancer survivors (Swainston & Derakshan, 2018) and in high anxious individuals (Sari et al., 2016), but not depression in a moderately dysphoric sample (Owens, Koster & Derakshan, 2013). There is however evidence that cognitive training can reduce depression (Hoorelbeke & Koster, 2017; Brunoni et al., 2014) and depressive rumination (Hoorelbeke et al., 2015; Siegle et al., 2014; Vanderhasselt et al., 2015) using other WM training paradigms with emotionally vulnerable and clinically depressed adult participants.

Reductions in anxiety and depression symptomology were evident not just at the end of the training period, but persisted at follow up, one month post intervention. This suggests that the positive effects of *n*-back training on emotional vulnerability were not short-lived and is evidence that adaptive training may have persistent lasting effects via cognitive plasticity in adolescence. Previously Swainston & Derakshan (2018) have shown that the positive effects of training persisted 18 month after intervention in a vulnerable adult population. Whilst our study suggests that sustainability of effects was also present here, further research using much longer-term follow up of adolescent participants is needed to address if the effects of *n*-back training would persist beyond one month.

No previous study has explored the impact of adaptive working memory training on depression and anxiety symptomology in a non-clinical adolescent population, and our study suggests a significant moderate effect of WM training on depression and anxiety. Anxiety and depression may have been reduced via an increase in cognitive control following training. Similar to adults (Borkovec, Robinson, Pruzinksy & DePree, 1983; Nolen-Hoeksema, 2000) repetitive negative thinking in the form of high levels of rumination and worry are characteristic of depression and anxiety in children and adolescents (Abela, Brozina & Haigh, 2002; Muris, Roelofs, Meesters & Boomsma, 2004; Schwartz & Koenig, 1996). Individuals with poorer attentional control may be prone to rumination and worry because of a greater susceptibility to intrusive negative thoughts, which are more difficult to control once worry or rumination has been initiated (Fox et al., 2015; Gotlib & Joorman, 2010). In this study, training may have increased attentional control reducing the prevalence of worrisome and ruminative thoughts. Although neither worry nor rumination were measured in this study, speculatively it may be the mechanism through which improvements in WM task performance reduced anxiety and depression.

The increase in WM following *n*-back training may have reduced anxiety and depression symptoms via improved top down regulation of worry and ruminative thoughts due to increased prefrontal regulation of amygdala activity. Siegle, Ghinassi & Thase (2007) and Siegle et al. (2014) demonstrated normalization of fronto-limbic disruption in depression after WM training. Recent studies indicate the likelihood of a fronto-parietal network providing a hub for flexible regulation across several brain regions, including limbic, motor and visual systems, in the service of goal-directed action (Cole, Repovš & Anticevic, 2014). In light of evidence of its disruption across diverse mental health disorders, Cole et al. (2014) propose the fronto-parietal control system as analogous to a psychological immune system. Healthy individuals may experience subclinical symptoms of anxiety and/or depression but successfully regulate symptoms via this fronto-parietal control hub. Of relevance to the current study, is that a central prediction of this hub system is that its integrity may be amenable to external manipulation via pharmacological or training interventions (Cole et al., 2014). Research on the neural correlates of WM and WM training suggest a potential overlap with this control hub. Evidence from functional and structural magnetic resonance imaging (MRI) and electroencephalography (EEG) has indicated that higher WM capacity is associated with greater fronto-parietal functional and structural connectivity (Constantinidis & Klingberg, 2016). Studies of the neural correlates of WM training indicate post-training changes in prefrontal and parietal cortical activity in adults and children (Klingberg et al., 2005; Olesen, Westerberg & Klingberg, 2004). Constantinidis and Klingberg (2016) reported increased fronto-parietal connectivity after WM training in children and suggested functional connectivity changes may result from myelination or stronger synaptic connectivity.

The behavioral and neural systems for WM undergo the most protracted development of all executive functions, not fully mature until late adolescence/early adulthood (Blakemore & Choudhury, 2006; Huizinga, Dolan & van der Molen, 2006; Luna, Padmanabhan & O'Hearn, 2010). Adolescence marks a critical period of maturation in the prefrontal cortex, which as previously described, is central to these systems. Increased vulnerability to mental health disorders in adolescence may be due to a culmination in maturational processes (Blakemore, 2008; Paus, Keshavan & Giedd, 2008). This vulnerability is also an opportunity. Whilst training interventions in adults target an established neural architecture, training interventions in adolescents may act upon systems under construction with a salutary influence on development (Galván, 2010; Jolles & Crone, 2012). As such, the results of the current study suggest improving working memory in adolescence may be a promising route for protecting against anxiety and depressive vulnerability in adolescents.

The current study extends previous research in several ways. It is one of few studies to investigate WM training amongst adolescents. Thus research on effects in adolescence, particularly in typically developing samples, is limited (Jolles & Crone, 2012; Karbach & Unger, 2014; Wass, Scerif & Johnson, 2012). It also extends research on a potential causal role for WM in the maintenance of anxiety and depression symptomology in healthy adolescents, and the potential for WM training in anxiety and depression prevention (Hoorelbeke et al., 2016). Finally, the sustainability of the effects of training on anxiety and depression are both novel and important and suggest the potential for adaptive *n*-back training to have lasting effects on mechanisms impacting cognition and emotion in adolescence.

4.2 Limitations

This study had a number of limitations. Participants were high academic achievers from independent schools. Generalizability to lower academic achievers needs caution. Secondly, there was poor training adherence and high attrition. It may be that the group who continued to train were self-selecting, thus biasing the results. However, equal numbers of participants were lost from each group, therefore any biases would apply to both intervention and control participants.

Whilst participants did not provide subjective feedback on their training experience, it is clear that many found it difficult to keep up their training over a prolonged period. This may be a reflection of the training task itself or a particular feature of undertaking intense cognitive training studies amongst adolescents, especially when participants have no clear incentives (participants were not paid in this study). Whilst parents might insist that younger children complete daily training exercises, this becomes more difficult as children enter adolescence and become less acquiescent to parental and experimenter wishes. This, combined with increased academic, extra-curricular and social commitments of adolescence, means daily training exercises may be low priority. This is hinted at in the negative association between age and training adherence in the present study. Future studies should improve how adolescent participants are incentivized to persevere in training interventions, whilst managing expectations regarding benefits of training itself and avoiding Hawthorne effects. This could include payment, although paying training participants is controversial and has been linked with lower rather than higher motivation and training effectiveness (Katz et al., 2018).

In the present study participants were briefed and recruited in fairly large groups and communications came via school staff rather than directly from researchers. Adherance might have been improved by a more ‘one-to-one’ relationship to promote a greater sense of participant’s personal responsibility. There is a fine line between encouraging participants who are falling behind in training and putting undue pressure on them. Perhaps more ethical would be better screening of participant motivation at the outset, however the cost might be an even more self-selecting sample. Alternatively, future researchers could develop better support systems to help participants anticipate and address boredom, loss of motivation or lapses in time management. In conclusion, motivation and adherence remain a major issue in this kind of study and future research should take this into account in study design and recruitment.

That not all participants entered into the analyses performed equal amounts of training is also limitation; however, our sensitivity analysis showed symptom change was not correlated with the number of completed training sessions. It is also important we acknowledge an additional limitation is that the analytic protocol and selection of a cut off at ≥ 6 days was not preregistered in this case. We do note however that these findings need to be replicated and any future replication attempts should be pre-registered. Finally, an attentional control measure and measures of worry and rumination would have permitted stronger conclusions on the mechanisms by which training WM might reduce anxiety and depression symptomology in adolescents. As it is, we may only speculate based on previous research that these mechanisms may have been involved.

4.3 Conclusion

Despite these limitations, the study's preliminary findings are nonetheless informative. This is one of few studies to explore the effects of WM training on cognitive vulnerability in typically developing adolescents, and to demonstrate not only positive effects on emotional vulnerability at the end of training, but also sustained effects at one month follow-up. The significant effects on depression is an important and novel finding. Previously, Takeuchi et al. (2014) showed that WM training compared to a non-active control reduced negative affect in healthy adults indicating a potential clinical application in promoting cognitive functioning to support mental wellbeing. The current study provides preliminary evidence that targeting cognitive vulnerability to anxiety and depression in adolescence via WM training is a viable area for further research. This is of particular relevance to how we might address vulnerability to developing internalising disorders amongst adolesecents in general, especially given widespread concerns about increasing prevalence of emotional disorders in this age group.

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Table and Figure Captions

Figure 1. The flow of participants through each stage of the study

Figure 2. Change in mean levels of *n*-back performance from day 1 to day 20

Figure 3. Changes in self-reported Total Anxiety symptomology as a function of training group across time

Figure 4. Changes in self-reported Total Internalising symptomology as a function of training group across time

Figure 5. Changes in self-reported Depression symptomology as a function of training group across time

Figure 6. Distribution of number of completed training sessions across participants

Table 1. Mean self-reported RCADS Total Anxiety, Total Internalising and Depression symptomatology, plus New Group Reading Test scores for groups (*n*-back and control) at pre-intervention (time 1) , post-intervention (time 2) and 1-month follow-up (time 3)

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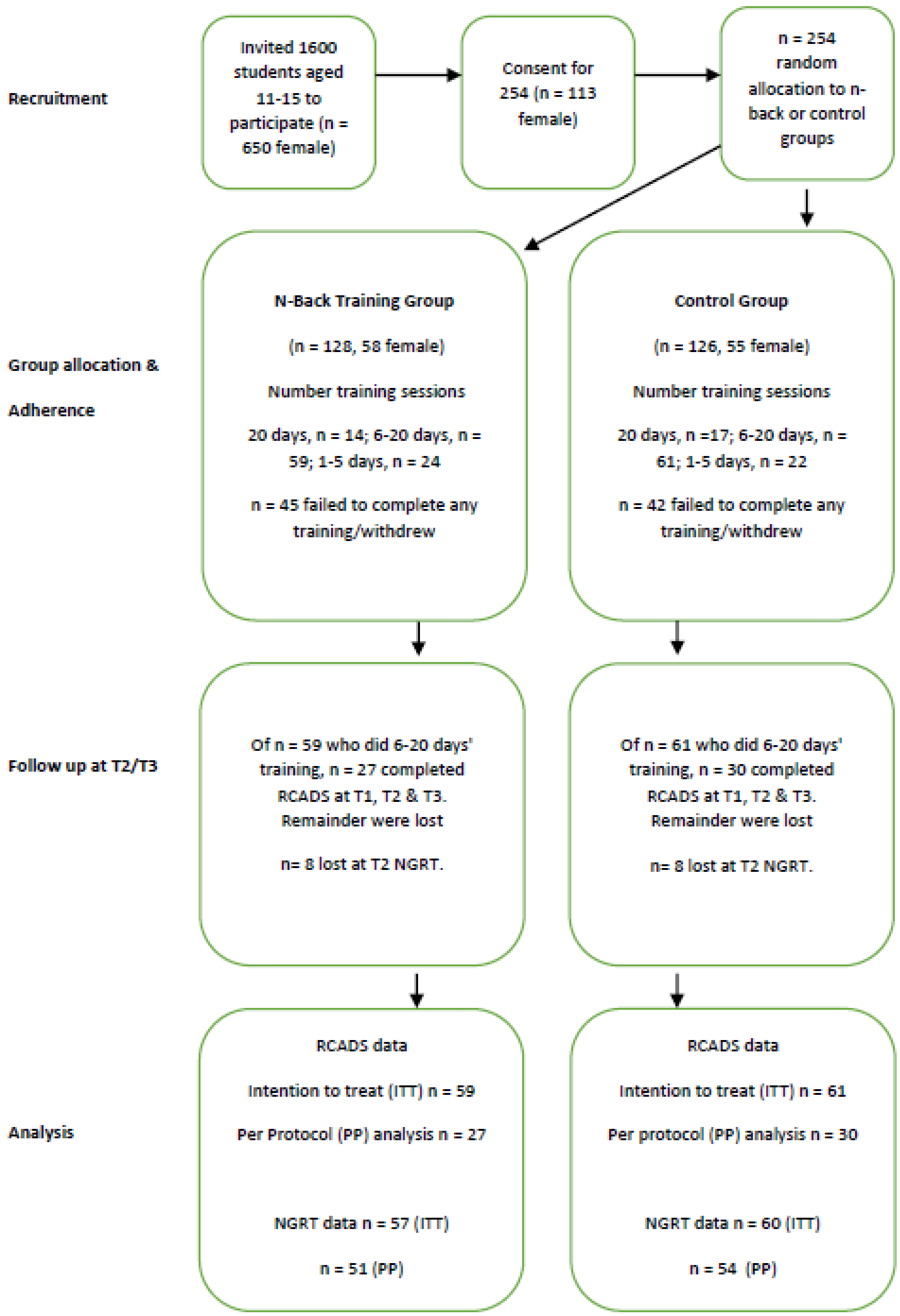
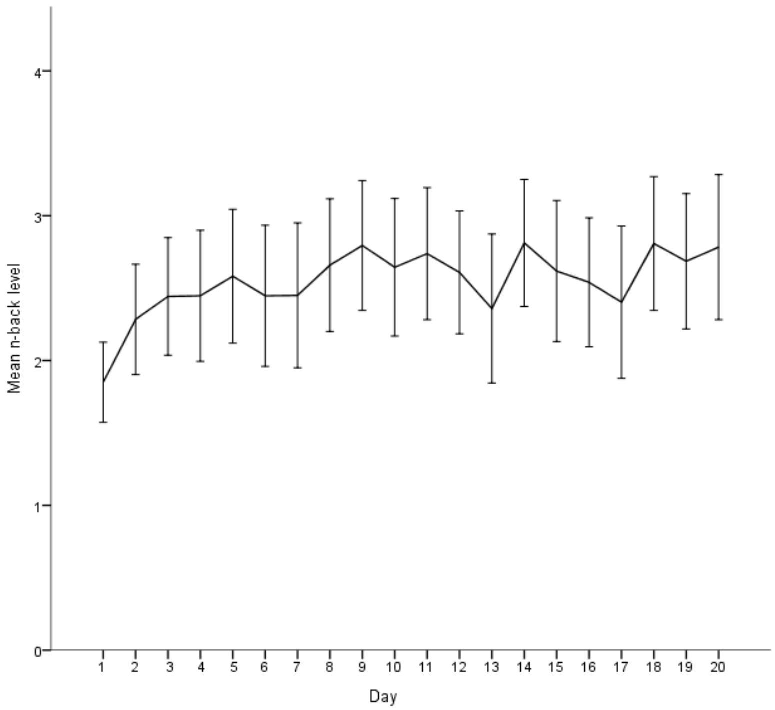


Recruitment
Invited 1600 students aged 11-15 to participate (n = 650 female)
Consent for 254 (n = 113 female)
n = 254 random allocation to n-back or control groups
Group allocation &
Adherence
N-Back Training Group
(n = 128, 58 female)
Number training sessions
20 days, n = 14; 6-20 days, n = 59; 1-5 days, n = 24
n = 45 failed to complete any training/withdrew
Control Group
(n = 126, 55 female)
Number training sessions
20 days, n =17; 6-20 days, n = 61; 1-5 days, n = 22
n = 42 failed to complete any training/withdrew
Follow up at T2/T3
Of n = 59 who did 6-20 days' training, n = 27 completed RCADS at T1, T2 & T3. Remainder were lost
n= 8 lost at T2 NGRT.
Of n = 61 who did 6-20 days' training, n = 30 completed RCADS at T1, T2 & T3. Remainder were lost
n= 8 lost at T2 NGRT.
Analysis
RCADS data
Intention to treat (ITT) n = 59
Per Protocol (PP) analysis n = 27
NGRT data n = 57 (ITT)
n = 51 (PP)
RCADS data
Intention to treat (ITT) n = 61
Per protocol (PP) analysis n = 30
NGRT data n = 60 (ITT)
n = 54 (PP)

Figure 1.



Error bars:95% CI

Figure 2.

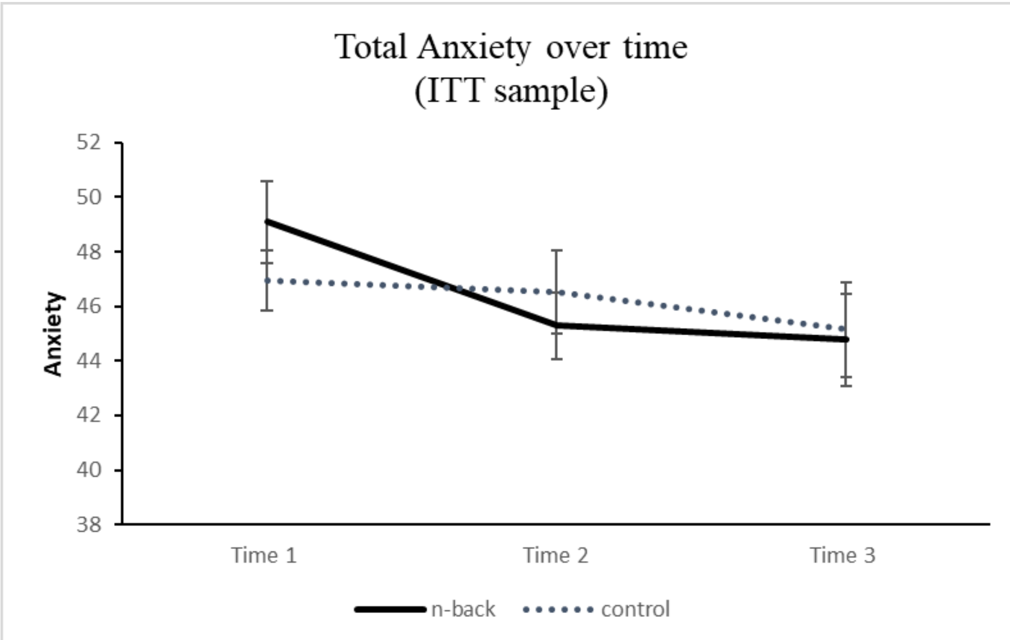


Figure 3.

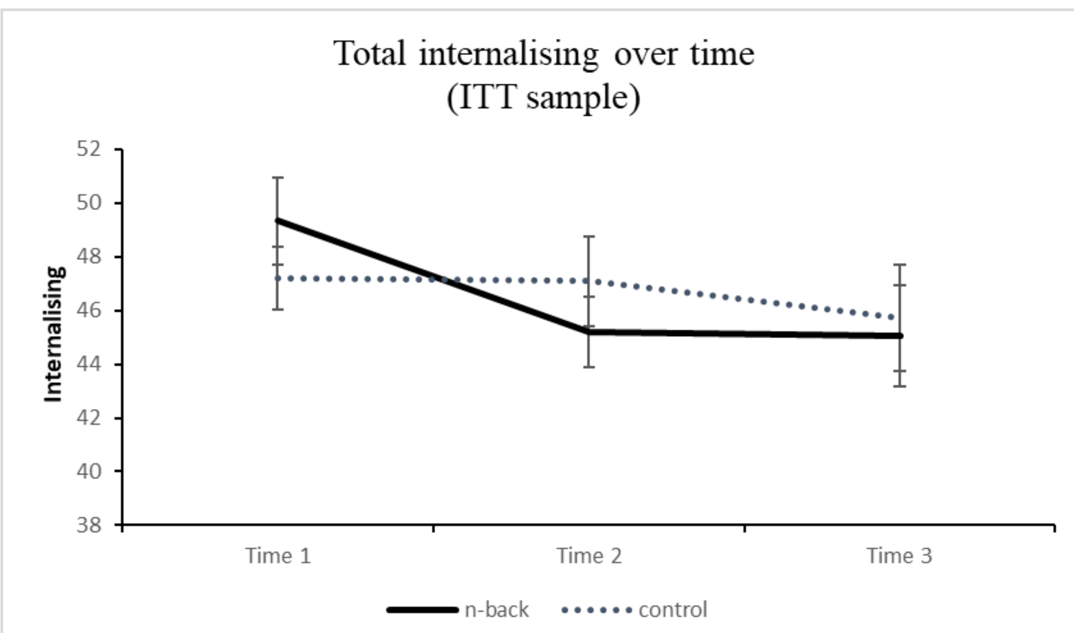


Figure 4.

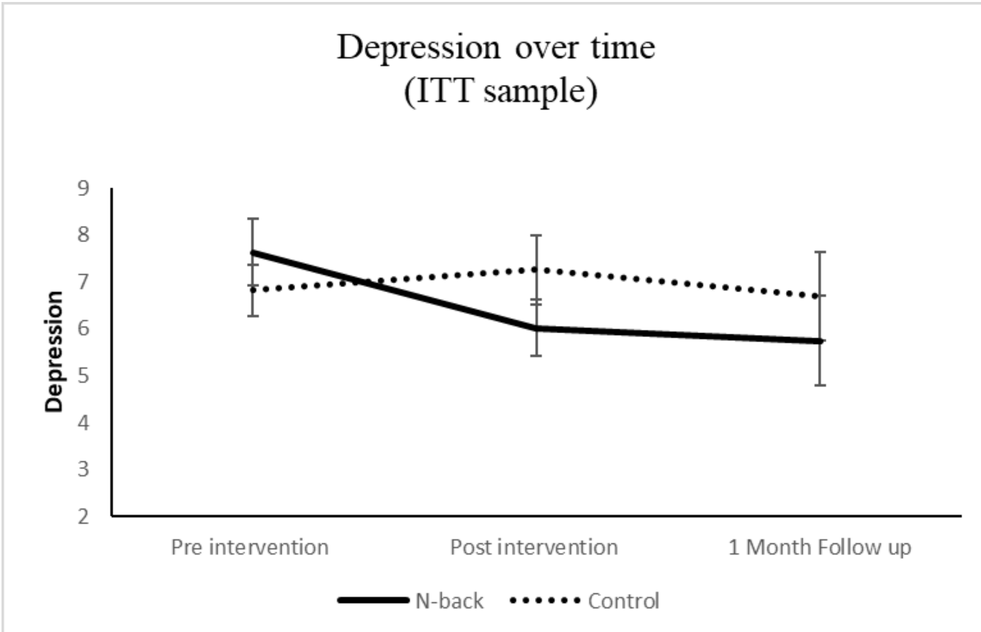


Figure 5.

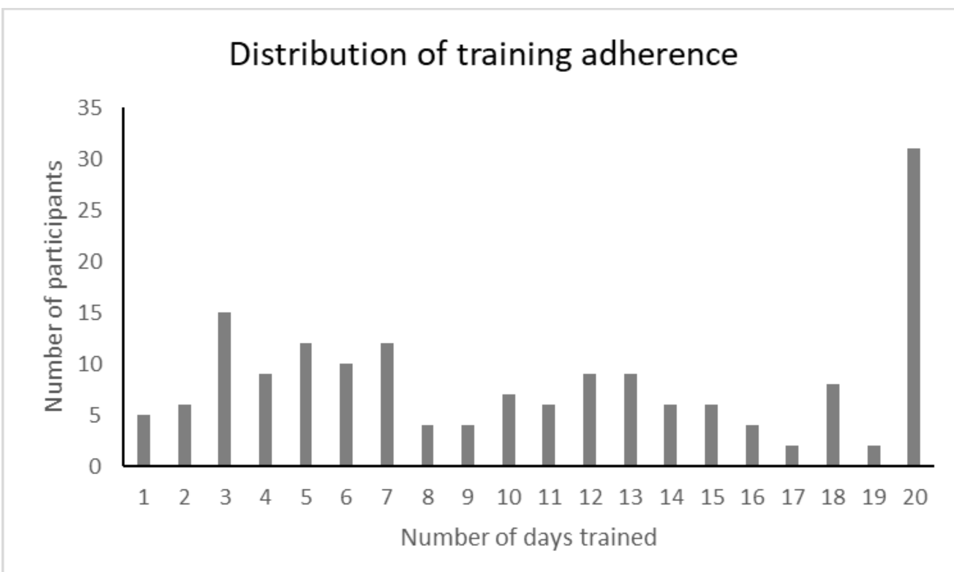


Figure 6

Table 1. Means and standard deviations (in parentheses) for self-reported RCADS scores for anxiety and depression symptomatology and NGRT reading for *n*-back and control groups at times 1, 2 and 3.

	Time 1		**Time 2**		**Time 3**	
	***N*-back**	**Control**	***N*-back**	**Control**	***N*-back**	**Control**
Anxiety (PP)	47.04 (8.62)	46.84 (9.34)	44.67 (8.89)	46.41 (11.6)	42.81 (7.62)	45.47 (10.80)
Anxiety (ITT)	49.08 (11.42)	46.9 (8.67)	45.28 (8.33)	46.54 (10.85)	44.77 (9.80)	45.14 (10.51)
Internalising (PP)	46.78 (9.65)	46.88 (10.01)	44 (9.48)	46.66 (12.66)	42.78 (8.58)	46.19 (12.19)
Internalising (ITT)	49.32 (12.3)	47.2 (9.24)	45.2 (8.83)	47.08 (11.84)	45.05 (11.00)	45.72 (11.90)
Depression (PP)	5.96 (4.08)	6.53 (4.87)	5.04 (4.26)	7 (5.54)	4.41 (4.01)	6.81 (5.92)
Depression (ITT)	7.64 (5.55)	6.82 (4.28)	6.02 (4.06)	7.26 (5.33)	5.73 (5.5)	6.7 (5.65)
NGRT	124.6 (7.48)	126.07 (9.03)	125.08 (7.93)	123.59 (13.07)	n/a	n/a