Improving attention control in dysphoria through cognitive training: Effects on working memory capacity and filtering efficiency

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Abstract

Impaired filtering of irrelevant information from working memory is thought to underlie reduced working memory capacity for relevant information in dysphoria. The current study investigated whether training related gains in working memory performance on the adaptive dual n-back task could result in improved inhibitory function. Efficacy of training was monitored in a change detection paradigm allowing measurement of a sustained event-related potential asymmetry sensitive to working memory capacity and the efficient filtering of irrelevant information. Dysphoric participants in the training group showed training related gains in working memory that were accompanied by gains in working memory capacity and filtering efficiency compared to an active control group. Results provide important initial evidence that behavioural performance and neural function in dysphoria can be improved by facilitating greater attentional control.

Keywords:
dysphoria, inhibition, working memory capacity, contralateral delay activity, adaptive dual n-back training, transfer
1. Introduction

Depression is a common and debilitating psychiatric disorder that poses a major challenge to mental health services due to its high prevalence and recurrence rate. However, limited effectiveness of interventions suggests that current psychopharmacological as well as psychotherapeutic treatments do not sufficiently target stable risk factors involved in depression (Kirsch, Deacon, Huedo-Medina, Scoboria, Moore, & Johnson, 2008; Cuijpers, Van Straten, Bohlmeijer, Hollon, & Andersson, 2011). Hence, it has been argued that more translational research is necessary to capitalise on improvements in the understanding of cognitive mechanisms underlying depression to develop new treatment strategies (De Raedt, Koster, & Joormann, 2010).

Cognitive control impairments are considered a crucial vulnerability factor for depression hampering emotion regulation and increasing stress reactivity (Joormann & D’Avanzato, 2010). There is evidence that cognitive control is impaired in depression with features such as impaired inhibition of negative information (Joormann, 2004), problematic updating of negative information (Joormann & Gotlib, 2008), as well as attentional and memory biases (De Raedt & Koster, 2010). Inhibitory dysfunction has been argued to underlie cognitive control deficits in depression (Joormann, Yoon & Zetsche, 2007). However, inhibition is difficult to measure precisely (Friedman & Miyake, 2004), which may contribute to inconsistent findings in the literature (e.g., Rogers, Kasai, Koij, Fukuda, Iwanami, Nakagome, Fukuda, & Kato, 2004). Recently, to explore inhibitory processes in depression in a more direct manner, we applied a neuroscientific approach focusing on the mechanisms and biological networks associated with inhibition (an approach proposed by, among others Aron, 2007; Dillon & Pizzagalli, 2007). Using a lateralized ERP technique developed by Vogel and colleagues (Vogel, McCollough, & Machizawa, 2005) we observed a depression-related impairment in the neural filtering of irrelevant information in visual
working memory that was associated with reduced capacity to maintain relevant information (Owens, Koster, & Derakshan, 2011).

In Owens et al. (2011) working memory capacity (WMC) was estimated by performance on a change detection task and compared between a sample of non-clinically depressed (dysphoric) university students and a control group of non-dysphoric students. Participants were asked to hold in memory either two or four oriented rectangles while ignoring two irrelevant rectangles of a different colour on some trials (distractor trials; two relevant/two irrelevant rectangles). Participants were assessed on their ability to detect whether or not target rectangles changed orientation across a short retention period. Non-dysphoric students were divided into high and low capacity groups based on accuracy and compared with the full dysphoric sample. It was found that WMC of dysphoric students was significantly lower than that of high capacity non-dysphorics, and was similar to that of low capacity non-dysphorics.

WMC as assessed by the change detection task shows a positive correlation with the ability to filter irrelevant information in visual working memory (Vogel et al., 2005). High capacity individuals selectively filter irrelevant items, whereas low capacity individuals tend to store irrelevant information thereby reducing available capacity for relevant information. The neural filtering of irrelevant information in the task is assessed by an event-related potential asymmetry termed contralateral delay activity (CDA). CDA amplitudes increase significantly according to the number of stored items (McCollough, Machizawa, & Vogel, 2007). Efficient neural filtering of irrelevant information is reflected in similar amplitudes between the distractor and two rectangle trials (mostly relevant items are stored). Imperfect filtering results in distractor amplitudes that are more similar to four rectangle trials (nearly all items are stored). Owens et al (2011) found that dysphoric and low capacity individuals had poor neural filtering of irrelevant visual distractors relative to high capacity individuals, a
finding that provided direct support for the long standing relationship proposed to exist between impaired inhibition and reduced working memory capacity in depression (e.g. Hasher & Zacks, 1988; Joormann et al., 2007).

Some recent research has shown that WMC in healthy participants can be improved through training (Jaeggi, Buschkuehl, Jonides & Perrig, 2008). Working memory training consisted of a dual $n$-back task in which participants were presented a sequence of paired audio and visual stimuli and determined whether either one or both of a currently presented pair matched those previously presented a selected number of trials ($n$) back in the sequence. Task difficulty was adjusted dynamically by increasing or decreasing $n$-back levels based on performance. Gains in WMC as a result of extended training (e.g. 17 and 19 days) had transfer effects on measures of adaptive reasoning (i.e. fluid intelligence). While, the neural mechanisms underlying training effects remain unclear (Buschkuehl, Jaeggi, & Jonides, 2012) it has been proposed that attentional control processes such as inhibition modulate individual differences in WMC (e.g. Engle 2002; Kane et al., 2001). Recent evidence has provided support for this view showing inhibitory-related function and working memory capacity are highly related in healthy and dysphoric samples (e.g. Vogel et al., 2005; Owens et al., 2011). So gains in WMC from adaptive dual $n$-back training may then indicate an underlying improvement to inhibitory processes, making it an ideal procedure to improve attentional deficits associated with depression (e.g. Gohier et al., 2009). It has been proposed that attentional control in depression can be facilitated experimentally (Hertel & Rude, 1991; Hertel, 1994). However, at present there is debate if training can result in a generalizable change to cognitive function (Shipstead, Redick, & Engle, 2012) so further research is necessary to determine if training can offer a means to improve executive function and WMC in depression.
As prospective studies indicate that cognitive control predicts depressive symptoms in at-risk samples (Zetschke & Joormann, 2011) as well as remitted depressed samples (De Meyer, Koster, De Lissnyder, & De Raedt, 2012) we set out to investigate whether cognitive control can be improved in a dysphoric sample. ERP techniques that examine attention and executive functions have the potential to facilitate novel developments in therapy for affective disorders; providing insight into mechanisms of action of treatment as well as to serve as predictors of outcome (Tamminga, Nemeroff, Blakely, Brady, Carter, Davis, et. al., 2002). Thus, the aim of the present study was to examine whether working memory training using the adaptive dual n-back could provide an effective means of increasing the neural filtering of irrelevant information in visual working memory and the capacity to maintain relevant information in dysphoric individuals. The present study was among the first to test the potential of cognitive training to facilitate a change in brain function for dysphoric individuals. We predicted that extended adaptive dual n-back training in dysphoric individuals would improve WMC and filtering efficiency measured at the behavioural and neural level, respectively.

2. Methods and Materials

2.1 Ethics

The current study was carried out under ethical guidelines, and approved by the research ethics committee of the Department of Psychological Sciences at Birkbeck University of London. Written informed consent was received from all participants before testing.
2.2 Participants

The study was advertised online through Birkbeck University of London and University College London automated experiment management systems. Similar to Owens et al. (2011) participants were initially pre-selected for the study based on their scores on the Beck Depression Inventory, BDI-II (Beck, Steer, Ball, & Ranieri, 1996). This inventory consists of 21 items assessing the severity of symptoms of depression. Each item has a four point scale ranging from 0 to 3. Participants were selected for the study if their score was greater than or equal to 20 as attention deficits tend to appear at a moderate level for the BDI-II within non-clinical samples (Rokke, Arnell, Koch, & Andrews, 2002). Including the initial pre-selected assessment of depressive symptoms (Time 1) participants were assessed two additional times on the BDI-II during the study, before their first EEG session (Time 2) and before their second EEG session (Time 3). 31 right-handed dysphoric participants were selected for study and allocated semi-randomly to training (adaptive dual n-back) and control group (dual 1-back) to match for gender and age. In the final sample, 11 participants were allocated to the training condition and 11 participants were allocated to the control condition. Participant demographics are listed in table 1. For the final sample the training group had lower initial BDI-II scores compared to the control group at Time 1, $F(1,21) = 4.20$, $p = .05$, and before their first EEG session (Time 2), $F(1, 21) = 8.08$, $p = .01$. The training and control groups did not differ on BDI-II scores before their second EEG session (Time 3), $F(1,21) = 3.76$, $p = .067$.

To control for group differences in BDI-II scores at Time 2, BDI-II scores were included as covariate in the analyses; and results showed that these group differences did not modulate the observed training effects (see results section 3.5.1 below for detail). The training and the control group did not differ on age, $F(1,20) = 2.63$, $p = .12$. 


2.3 Study Design

The study was conducted across a maximum of two weeks (minimum eleven days), and was composed of two EEG sessions separated by a period where participants completed testing an online dual n-back task at home. At the end of the first EEG session participants were informed of the testing structure, and given an introduction to the dual n-back task. Participants completed eight days of testing on the dual n-back task. The participants in the training group completed an adaptive version of the dual n-back, while participants in an active group control completed a non-adaptive dual 1-back task; see section 2.5.6 for details of each task. The day after n-back testing participants completed their second EEG session. Participants were paid £37 for approximately six experimental hours.

2.4 Materials and Procedure

2.4.1 Change Detection Task

Stimuli were presented on a 17inch LCD with a refresh rate of 16.6ms. The experimental task was programmed and run using DMDX programming software (Forster, & Forster, 2003) on a Dell Optiplex GX520. The change detection task was the same used in Owens et al. (2011) and was originally reproduced from Vogel et al. (2007). In the task participants were presented with trials consisting of two stimulus arrays, a memory array, and a test array. Participants were instructed to remember the orientations of target items (red rectangles) from the memory array across a short retention period. Accuracy was then assessed during the test array. On half of the trials the orientation of one red rectangle changed from the memory array to the test array, on the other half no change in orientation
occurred for any rectangle. In the test array participants responded with one of two button presses to indicate whether the orientation of one of the red rectangles changed or did not change. Stimuli were viewed at a distance of 60cm. Each array consisted of two or four rectangles (0.64° x 1.21°) spaced at least 2° apart and positioned randomly within a 4° x 7.2° rectangular region. Regions were centred 3° from a white central fixation cross on a black background. Each rectangle was oriented randomly along one of four positions (vertical, horizontal, left 45°, right 45°) and the colour could be either red (target rectangle) or blue (distractor rectangle) depending on trial condition.

Each trial (see Figure 1) began with a central fixation, and a white arrow above, pointing either to the left or right, that remained on screen for 700ms. Participants were instructed to maintain fixation during each trial and attend to the side indicated by the arrow. After presentation of the cross and arrow, on both sides of the fixation, arrays of either 2 red rectangles (two item condition), 4 red rectangles (four item condition) or 2 red rectangles and 2 blue rectangles (distractor condition) were presented for 100ms (memory array). All rectangles were then removed from the display for 900ms (retention period) and then redisplayed for 2000ms (test array). The intertrial interval was varied randomly between 1500 and 2000ms.

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Array size (conditions: two item, four item & distractor condition), arrow direction (left & right), change and no change trials were randomized and presented equally often across the experiment. Participants completed a short practice phase consisting of 24 trials (8 per condition) before the experimental blocks. The experiment was split into 7 blocks of 84 trials (196 trials per condition), totalling 588 trials across the experiment. Within each block
participants were given a short break after half of the trials were completed. Each experimental session lasted approximately 60 minutes.

2.5 Data preparation

2.5.1 Working memory capacity

Each participant’s WMC was estimated from their performance on the change detection task using a standard formula typically used for this paradigm (Cowan, 2000; Vogel et al., 2005). The formula is $K = S(H-F)$, where $K$ is the WMC, $S$ is the size of the array (i.e., 4 or 2), $H$ is the hit rate or proportion of correct responses when a change is present, and $F$ is the false alarm rate or the proportion of incorrect responses when no change is present. In line with previous studies (e.g. Lee, Cowan, Vogel, Rolan, Valle-Inclan & Hackley, 2010) we used $K$ scores in the 4 item condition to estimate WMC rather than an estimate consisting of an average across conditions; this allowed exclusion of variance from ceiling or floor level performance in the 2 item or distractor condition.

2.5.2 EEG recording

Participants were seated in an electrically isolated, sound proof room with dimmed lighting. EEG was recorded using 64 Ag/AgCl sintered ring electrodes mounted on a fitted cap (EASYCAP) according to the international 10/20 system. The horizontal electrooculogram (EOG) was recorded from two electrodes placed 1 cm to the left and right of the external canthi to measure horizontal eye movements. Vertical EOG was recorded from a single electrode placed below the left eye to measure eye blinks. Electrode impedance was kept below 5 kΩ. EEG data was recorded referenced to the left mastoid, and re-referenced offline to the mean of the left and right mastoids (average mastoids). EEG
recordings were amplified and filtered with a Brain AMP standard model amplifier (Gain: 1000) with a bandpass at 0.01–80 Hz and sampled at 250 Hz.

2.5.3 EEG processing

EEG data was processed in two stages using the MATLAB extension EEGLAB (Delorme & Makeig, 2004) and the EEGLAB plugin ERPLAB (Lopez-Calderon & Luck, 2010). EEG data was processed using both artifact correction and rejection. First independent component analysis (ICA) was conducted to identify and remove stereotypical ocular, muscle, and noise components (Jung, Makeig, McKeown, Bell, Lee, & Sejnowski, 2001). Artifact detection and rejection was then conducted on epoched uncorrected data files to identify and remove trials containing blinks and large eye movements at the time of stimulus presentation. Trials with ocular artifacts at stimulus presentation were removed from both behavioural and ICA corrected continuous data. For the first EEG session the mean number of trials remaining after artifact rejection for each group was: $M = 536$ ($SD = 39$) for the training group and $M = 537$ ($SD = 29$) for the control group. For the second EEG session the number of trials remaining after artifact rejection for each group was: $M = 547$ ($SD = 38$) for the training group and $M = 518$ ($SD = 35$) for the control group. Groups did not significantly differ in trials remaining either the first, $t < 1$ or second EEG session, $t(20) = 1.95$, $p > .05$.

2.5.4 Contralateral Delay Activity (CDA)

CDA is a large negative voltage over posterior regions contra-lateral to the position of the to-be-remembered items on the display. CDA is computed as the difference in mean amplitude between activity in hemispheres contralateral and ipsilateral to the memory array during the retention period. Activity from posterior electrode sites (P1/2, P3/4, P5/6, P7/8, PO3/4, PO7/8, O1/2) within the time period of 300–900 ms after onset of the memory array was used in the calculation of CDA. Contralateral waveforms were calculated by averaging
activity recorded at right hemisphere electrode sites when participants were cued to remember items on the left side of the central fixation with activity recorded from the left hemisphere electrode sites when participants were cued to remember items on the right side of the central fixation. Conversely, ipsilateral waveforms were calculated by averaging the activity recorded at right hemisphere electrode sites when participants were cued to remember items on the right side of the central fixation with activity recorded from the left hemisphere electrode sites when participants were cued to remember items on the left side of the central fixation.

2.5.5 ERP analysis – filtering efficiency

Filtering efficiency scores were derived from CDA waveforms averaged across posterior electrode sites (P1/2, P3/4, P5/6, P7/8, PO3/4, PO7/8, O1/2) within the time period of 300–900 ms after onset of the memory array. The amplitude of CDA is sensitive to the number of items remembered for each trial; increasing significantly between arrays of up to four items (McCollough et al., 2007). The sensitivity of CDA makes it suitable to accurately determine the efficiency of inhibitory processes during the task. Analysis of CDA used a formula to compute a ratio score that represented each participant’s ability to efficiently filter irrelevant information (Vogel et al., 2005). The formula provides a quantitative measure of whether mean amplitudes of CDA on the distractor condition are more similar to that of the four items, suggesting irrelevant information was inefficiently stored in working memory, or two items condition, suggesting irrelevant information was efficiently filtered. Scores range from 1 (efficient: identical to two item) to 0 (inefficient: identical to four item). The formula is, \( FE = \frac{(F-D)}{(F-T)} \), where FE is filtering efficiency, F is the amplitude for four items, D is the amplitude in the distractor present condition (blue rectangles present in display) and T is the amplitude in the two items condition\(^2\).
2.5.6 Dual N-Back Task.

We used a standard dual $n$-back task shown to improve working memory function (Jaeggi et al., 2008). In the task participants were presented green squares that could appear at one of eight different locations within a 3 by 3 grid. A cross in the centre of the grid served as a central fixation. Simultaneously with presentation of the green squares one of eight consonants (c, h, k, l, q, r, s, and t) was spoken (see Figure 2). Audio and visual stimuli were presented sequentially at rate of 500ms, and each trial was separated by a 2500ms interval trial interval. Participants were instructed to remember the location of the green square within the grid and the letter spoken for each trial. Participants responded whenever either of the presented stimuli matched a letter spoken or location of the green square within the grid presented ($n$) trials back in the sequence. Participants made responses manually by pressing on the “A” letter for visual targets and “L” for auditory targets. No responses were required for non-targets. For trials with both visual and auditory matches participants were instructed to press both “A” and “L” buttons simultaneously. Participants were instructed to be as fast and accurate as possible.

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Participants completed the dual $n$-back task at home over the internet on a website designed specifically for the study and monitored by the experimenter. On the first day of testing both the control and training groups completed a single practice block (20 trials) on the dual 1-back level. After this first day participants were given only experimental blocks. Homework for each day consisted of completing 20 blocks of 20 trials (the training group completed 20 + $n$ trials each day, see below for description). Each block lasted approximately 1 minute. Targets were set semi-randomly to ensure each block had an equal number of
visual and audio matches (4 per block). Additionally blocks also contained 2 trials where both the audio and visual stimuli matched stimuli $n$-trials back. Target positions within each block were determined pseudo-randomly to ensure the value of $n$ was the same for both steams of stimuli. Short breaks were given between blocks (15s). The game could not be paused after starting so participants were instructed to remain at their computer during each testing session. One homework session took approximately 30 minutes.

Significant performance increases in working memory have been observed to occur after 8 days of training (Jaeggi et al., 2008) suggesting adaptive dual $n$-back training can be beneficial even across relatively short periods. Participants in our study conducted the training across 8 weekdays with two day breaks across weekends. Participants completed a minimum of four days of training per week. Performance was monitored by the experimenter and participants received an online summary of their percentage scores for each modality across blocks after each session. The dual $n$-back task has been argued to facilitate the use of executive processes from 2-back (Jaeggi et al., 2007), yet remains relatively challenging at the 1-back level as a result of dividing attention across parallel streams of stimuli. As such, the dual $n$-back is a useful paradigm to train executive function, and allow comparison to an active control group. For the current study participants in the training group completed a version of the dual $n$-back task in which the highest level that could be reached on a given day was 4-back, for the control group only the dual 1-back was given. In the training condition participants were encouraged to try to reach and maintain the highest level they could each day. The control group was encouraged to reach and maintain the highest percentage scores possible for the audio and visual stimuli they could each day.
2.5.6.1 Procedure for the Training Condition

For each session, participants in the training group completed 20 blocks of 20 + $n$ trials ($n$ was determined by the level of $n$-back, e.g. 3-back, $20 + 3 = 23$ trials). Within the training condition the level of difficulty ($n$-back level) was varied using percentage scores based on average accuracy (hit rate minus false alarm rate) for each modality (i.e. visual and auditory) after each block. On each day of training participants started on the 1-back level. We chose specifically to start each day at an easy level in order to limit the task being perceived as too demanding and to avoid the training being a failure experience. After the first block the level of $n$ was increased by 1 if accuracy was at or above 95% for each modality (audio & visual). The level of $n$ was decreased by 1 if performance was below (for either modality) 75%, $n$ remained unchanged if participants scored between 75-95%. After eight days of training participants typically average a 4-back level (Jaeggi et al., 2008), so this level was set as the highest $n$-back level in the study. Before each block the upcoming level was displayed on screen during breaks, and remained visible throughout the block.

2.5.6.2 Procedure for the Control Condition

Within the control condition the level of difficulty did not vary. Participants completed 20 blocks of 20 trials per day. Control participants only took the dual 1-back during the period between EEG sessions as this level has been shown to have significantly lower DLPFC activation relative to the 2-back condition, suggesting less controlled processes are engaged (Jaeggi et al., 2007). This procedure was implemented to control for unspecific experimental effects (Buschkuehl & Jaeggi, 2010), ensuring that the control group remained active, and performed a task as similar as possible to the training group with the exception of levels that greatly rely on working memory processes.
3. Results

3.1 Dual n-back Performance

Homework performance was analysed for the training group to ensure that participants complied with the instructions to perform the tasks at home and to examine the amount of improvement across sessions. Accuracy (hit rate minus false alarm rate) was averaged across visual and audio stimuli to assess performance for the control group across homework sessions. Mean accuracy for the control group indicated good performance across homework sessions ($M = 87.75\%, \ SD = 6.81\%$) for the dual 1-back.

3.1.1 Adaptive Dual N-Back Training

In accordance with previous research (Jaeggi et al., 2008) the first three trials were excluded from analysis to calculate the participant’s actual training level for each day. Participants in the training group showed improved working memory, as measured by mean dual $n$-back level, between the first ($M = 1.54, \ SD = 0.49$) and last ($M = 2.46, \ SD = 0.91$) training session, $t(10) = 4.12, \ p = .002$. Mean dual $n$-back level for the training group by training day is shown in Figure 3.

3.2 Change Detection Performance

Mean WMC (4 item condition) and FE scores from first EEG session and the second EEG session for each group are listed in Table 2. To ensure participants did not differ in initial WMC an ANOVA was conducted with group (training, control) as between subject factor and WMC as the dependent factor. Neural activity was examined in two stages; first
CDA amplitudes were analysed for typical differences between the two item, four item and
distractor condition to assess their ability to capture maintenance of the items in visual
working memory. Formal analysis of CDA was then conducted using FE calculations. To
examine initial filtering ability an ANOVA was conducted with group (training, control) as
between subject factor and FE as the dependent factor

3.2.1 WMC

3.2.1.1 Time 2 (pre-test)

Training and control groups did not differ in initial WMC, $F<1$ showing both groups
performed similarly on the change detection task during their first EEG session.

3.2.2 CDA and FE

3.2.2.1 Time 2 (pre-test)

Figure 4a shows grand mean CDA waveforms by condition for the training and
control groups averaged across posterior electrode sites during first EEG session (Time 2).
Waveforms for each group show that within the 300-900ms time window CDA amplitudes
were highest for the 4 item array followed by the distractor condition and 2 item conditions.
A mixed ANOVA was conducted with Group (training, control) as between subject factor
and Condition (2 item, distractor, 4 item) as within subject factor. As assumptions of
sphericity were violated Greenhouse Geisser corrected values are reported. Analysis yielded a
main effect of Condition on CDA amplitudes, $F(2,40) = 62.61, p < .001$. Table 3 lists mean
CDA amplitudes for the first EEG session and second EEG session for each group. In line with previous studies (e.g., McCollough et al., 2007) CDA amplitudes were significantly different between all conditions ($ps < .001$, Bonferroni corrected) indicating that CDA amplitudes were sensitive to the number of representations held in visual working memory (4 item > 2 item condition). Participants also did not completely filter the distractors (distractor condition > 2 item condition) storing at least some irrelevant information during the retention period. There was no Group X Condition interaction $F(2,40) = 1.58, p = .22$, suggesting that initial filtering efficiency was similar for both groups. Formal analysis of CDA using FE calculations showed training and control groups did not differ significantly in initial inhibitory function, $F<1$.

3.3 WMC and FE Relationship

3.3.1 Time 2 (pre-test) and Time 3 (post-test)

Similar to previous studies (Vogel et al., 2005) we observed a significant positive correlation between WMC and FE across all participants at Time 2 during their first EEG session, $r(22) = .67, p = .001$, see Figure 5a. The positive correlation between WMC and FE remained at Time 3 in the second EEG session, $r(22) = .60, p = .003$, see Figure 5b.
3.4 Transfer effects

Both groups showed similar WMC and FE at Time 2 (first EEG session). It was predicted that as a result of adaptive dual n-back training the training group would show larger gains in WMC and FE at Time 3 (second EEG session) relative to the active control group who completed the non-adaptive dual 1-back task. Two separate ANCOVAs were performed on Time 3 WMC and FE scores respectively, with group (training, control) as the between subject factor and Time 2 WMC and FE scores as the covariate (c.f. Weinfurt, 2000). WMC scores at Time 3 were found to be significantly larger for the training group (M = 2.36, SD = .62) versus the control group (M = 1.85, SD = .56), F(1,19) = 7.63, p = .01, when controlling for WMC scores at Time 2. FE scores at Time 3 were found to be significantly larger for the training group (M = .58, SD = .11) versus the control group (M = .47, SD = .18), F(1,19) = 5.90, p = .02, when controlling for FE scores at Time 2. These results indicate that change detection performance improved to a significantly greater degree for the training group (WMC gain, M = .57, SD = .36) relative to controls (WMC gain, M = .22, SD = .37), d = .9, see figure 6a. In a similar manner, filtering efficiency improved to a significantly greater degree for the training group (FE gain, M = .18, SD = .15) relative to the control group (FE gain, M = .03, SD = .16), d = .9, see figure 6b.

Insert Figure 6a and 6b Here

Training participants, compared to the control participants, had lower scores on the BDI-II at Time 2. In order to rule out that any gains in WMC and FE attributed to training may have been affected from differences in reported levels of dysphoria at Time 2, we conducted two separate one way ANCOVAs with group (training, control) as between
subject factor, gain scores (FE or WMC) as the dependent variable, and BDI-II scores at Time 2 as the covariate. There was no main effect of BDI-II for WMC: $F < 1$, or for FE: $F(1, 19) = 1.16, p = .2$. Importantly, the main effect of group was still significant for WMC, $F(1, 19) = 4.09, p = .05$ and FE, $F(1, 19) = 5.81, p = .02$ after controlling for BDI-II scores at Time 2, suggesting that performance gains were related to training.

### 3.5.2 Additional EEG analyses

CDA amplitudes for the control group were lower at Time 3 versus Time 2 (see table 3). Low CDA amplitudes have been interpreted as reflecting reduced storage capacity (Lee et al., 2010). However, the control group showed improvement in WMC across EEG sessions suggesting reduced capacity was not the cause of lower CDA amplitudes at Time 3. Early-evoked spatial attention (P1/N1) may affect interpretation of CDA amplitudes (Fukuda & Vogel, 2009). Voluntary attention was assessed to rule out the possibility that the control group did not adequately oriente spatial attention to the cued location at Time 3. Voluntary attention was measured as the difference between contralateral activity and ipsilateral activity from 75 – 175ms (P1/N1) after onset of the memory array at posterior electrode sites (P3/4, P7/8, PO3/4, PO7/8, O1/2) (Fukuda & Vogel, 2009). Mean amplitudes were compared between groups (training, control) and within condition (2 item, 4 item, distractor) using a mixed ANOVA. P1/N1 amplitudes did not differ by condition $F < 1$ nor was there a significant interaction between condition and group, $F(2, 40) = 1.01, p > .2$. Additionally, there was no significant relationship between P1/N1 amplitudes and WMC, $r(22) = -.12, p > .4$ at Time 3.

Between the first and second EEG sessions (Time 2, Time 3) the training group showed increases in CDA amplitudes while the control group showed decreases; such changes may have implications for the interpretation of the training manipulation, e.g.
increases or decreases in CDA amplitudes across EEG sessions may have been associated with changes in FE for the training or control group. A mixed ANOVA with Group as the between subject factor and Time (Time 2, Time 3) and Condition (2 item, 4 item, distractor) as within subject factors was conducted to investigate this issue. There was a significant Group X Time X Condition interaction, $F(2,40) = 6.75, \ p = .003$. This interaction showed that changes in CDA amplitudes from the first and second EEG session (Time 2 CDA minus Time 3 CDA) were significant between groups for the four item, $t(20) = 3.16, p = .005$ and distractor condition, $t(20) = 2.24, \ p = .03$, but not the two item condition, $t(20) = 1.24, p > .2$. Importantly, differences between CDA amplitudes at Time 2 and Time 3 for each condition were not correlated with gains in FE (FE Time 3 minus FE Time 2) for either group, all $p$’s $> .09$. Together, additional EEG analyses suggest that performance was unrelated to spatial attention and the ability of CDA to assess FE is robust against variation in EEG signals across sessions.

4. Discussion

There is evidence that fundamental executive dysfunction underlies cognitive deficits and impaired emotion regulation in depression, with proposals arguing that such deficits can be alleviated through greater attentional control (Hertel, 1994; Joormann et al., 2007; Levin, Heller, Mohanty, Herrington & Miller, 2007). Yet little research has been devoted to applying these basic findings to guide remediation (Siegle, Ghinassi & Thase, 2007; Tamminga et al., 2002; Linden et al., 2012). The results of the current study have provided important initial evidence that executive function in depression is amenable to training procedures that facilitate attentional control processes. Importantly, improvements are transferrable across tasks. Implications of the findings and directions for future research are discussed below in relation to translational research in depression.
Consistent with previous training research (Jaeggi et al., 2008) we observed significant improvement in working memory performance over time. This occurred across a testing period of eight days for moderately dysphoric individuals suggesting the adaptive dual n-back is an effective means for improving WMC in non-clinical samples generally low in attentional control and overall cognitive performance (Owens et al., 2011). The transfer of training effects on attentional control in the present study appears substantial as the dual n-back and change detection task differed on many levels. Thus, adaptive dual n-back training in dysphoric individuals seems to elicit a generalizable change in cognitive ability (Shipstead, Redick & Engle, 2010). As there is debate about the effectiveness of working memory training (Shipstead et al., 2012) our study provides an important proof-of-principle that training on the adaptive dual n-back task can improve WMC.

Importantly, results of the current study demonstrate a change in depression-related cognitive impairments at behavioural as well as neural levels of measurement. Specifically, a significant increase was observed for the training group in both the neural filtering of irrelevant information as well as WMC in Time 3, relative to controls. WMC and filtering efficiency showed a significant positive correlation in both EEG sessions and spatial attention was unrelated to working memory capacity at Time 3. As such, results provide further support that misallocation of attentional resources to irrelevant information drives individual differences in WMC (Vogel et al., 2005). Findings are also in line with theoretical proposals and recent neural evidence linking inhibition and working memory (Hasher & Zacks, 1988; McNab & Klingberg, 2008). In their fMRI study, McNab & Klingberg (2008) observed that activity in the prefrontal cortex and basal ganglia preceded the filtering of irrelevant items in the posterior parietal cortex and this in turn predicted inter-individual differences in visual working memory capacity.
Recent research has demonstrated that training leads to increased functional and structural connectivity in frontal and parietal regions (Jolles, van Buchem, Crone & Rombouts, 2011; Takeuchi et al., 2010). However, there is still uncertainty as to what neural mechanisms underlie working memory training (Buschkuehl, Jaeggi, & Jonides, 2012). Our results imply that training facilitates improvement for inhibitory-related prefrontal and subcortical functions involved in the maintenance of relevant information and removal of irrelevant information in working memory (Banich, 2009; O’Reilly, 2006). As such, our findings complement previous research that has shown training results in physiological changes. Additionally, there is preliminary evidence that the typical transfer gains are stable as gains in fluid intelligence associated with adaptive training remain after a period of 3 months in children (Jaeggi, Buschkuehl, Jonides & Shah, 2011). Together recent studies suggest training may be useful to facilitate sustainable changes to neural mechanisms associated with attentional control. Future research should determine if training can result in the long term improvement of inhibitory function for dysphoric or depressed adults.

Although the results of the current study were obtained from a non-clinical sample they indicate the promise of this line of research for therapeutic techniques that seek to enhance attentional control in depression (Siegle et al., 2007). It has been argued that improving executive impairment may prove to be a crucial first step in the treatment of depression, as it is often difficult to move forward with interventions as these impairments hamper normal functioning (concentration and memory problems) and, thus, verbal psychotherapy (Baert, Koster & De Raedt, 2011). In line with models of vulnerability to depression (Just, Abramson & Alloy, 2001; Mathews & MacLeod, 2005) this study hypothesized that effects of cognitive processes on symptoms are more indirect; manifesting through interactions with stress reactivity and emotion regulation. A very recent study suggests that targeted neurofeedback training increases activity in brain areas associated with
positive emotion processing which can in turn reduce symptoms of depression across a period of 6 weeks (Linden et al., 2012). Future research should examine whether working memory training alone or in combination with neurofeedback training would be a useful alternative or adjunct to existing treatments for improving attentional control and reducing levels of depression.

There are some restrictions to the current study. First, the sample size of the study was relatively small; however, the effect sizes for the observed differences between groups for gains in WMC and FE were large, suggesting that the obtained effects were genuine. Second, as stated earlier, the main aim of this investigation was to examine the effects of training on fundamental inhibitory processes rather than symptoms of depression. In fact we did not observe an effect of training on self-reported depressive symptoms as measured by the BDI-II. Notably, a reduction in depressive symptomatology would necessitate a longer time-line of training with the impact of critical life events and self-regulation strategies also considered in this process (e.g. Just et al., 2001; Linden et al., 2012). Third, the training group had lower BDI-II scores at Time 2 relative to controls. However, there is no evidence that the training group was less impaired than the control group as no significant differences between groups were observed for WMC and FE at Time 2. As there were differences in BDI-II scores at Time 2, we first made sure that for the analyses of FE and WMC there were no corresponding differences at Time 2 between both groups. Importantly, no differences are observed. Nevertheless, as depression levels could influence the malleability of cognitive impairments, we included depression scores as covariates in further analysis; and this showed that BDI-II scores were unrelated to gains in performance for both WMC and FE. Fourth, we deliberately chose to conduct the current study in non-clinically depressed individuals as the training was cognitively challenging and it was unsure whether it was suitable for clinically depressed individuals. Recent reports have indicated that the single adaptive n-back is as effective as
that dual $n$-back for improving fluid intelligence (Jaeggi, Studer-Luethi, Buschkuel, Su, Jonides, and Perrig, 2010) suggesting working memory training can be applicable to populations for which the dual $n$-back would be too difficult. Finally, the study did not consider the influence of anxiety on performance for dysphoric participants and given high comorbidity between these states it will be important for future research to examine whether state or trait anxiety was associated with differences in working memory training, and changes to FE and WMC.

5. Conclusion

In conclusion, using a well-studied change detection paradigm allowing for the direct estimation of WMC and inhibitory function (Vogel, Woodman & Luck, 2001; Vogel et al., 2005) it was found that WMC and the neural filtering of irrelevant information in dysphoria can be significantly improved through working memory training. Results suggest that utilizing the adaptive dual $n$-back task can have an effect on neural and behavioural measures of attentional control which may have implications for interventions that seek to reduce the cognitive and emotional symptoms of depression.
References


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Author Notes

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Footnotes

1. Data Analysis A total of 9 participants are not included in analyses. Five participants (N = 2 training group, N = 3 control group) declined to finish the study after the first EEG session and participants with total BDI-II scores below 11 during either re-assessment were excluded (N = 2 control). Additionally, within the training group 2 participants was removed due to difficulty understanding the training task.

2. Calculation of filtering efficiency (FE) can produce outliers if mean CDA amplitudes for the 2 item condition are, for example, greater than the 4 item condition (i.e. negative FE). However, all participants in the current study had FE scores within the range of 0 to 1 so were included in the analysis.
Table 1

Participant demographics, and BDI-II assessment scores (standard deviation)

<table>
<thead>
<tr>
<th>Group</th>
<th>Age</th>
<th>Gender (Female/Male)</th>
<th>BDI-II Time 1</th>
<th>BDI-II Time 2</th>
<th>BDI-II Time 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Training</td>
<td>27.72 (5.33)</td>
<td>(6/5)</td>
<td>24.81 (3.40)</td>
<td>19.45 (4.84)</td>
<td>17.00 (6.40)</td>
</tr>
<tr>
<td>Control</td>
<td>22.63 (3.38)</td>
<td>(8/3)</td>
<td>30.27 (8.13)</td>
<td>27.18 (7.60)</td>
<td>23.81 (9.73)</td>
</tr>
</tbody>
</table>
Table 2

Mean WMC (4 item condition) and FE for the first EEG session (Time 2) and the second EEG session (Time 3) by group. Standard deviations are in parenthesis.

<table>
<thead>
<tr>
<th>Group</th>
<th>WMC Time 2</th>
<th>WMC Time 3</th>
<th>FE Time 2</th>
<th>FE Time 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Training</td>
<td>1.78 (.78)</td>
<td>2.36 (.62)</td>
<td>.40 (.20)</td>
<td>.58 (.11)</td>
</tr>
<tr>
<td>Control</td>
<td>1.63 (.53)</td>
<td>1.85 (.56)</td>
<td>.43 (.17)</td>
<td>.47 (.18)</td>
</tr>
</tbody>
</table>
Table 3

Mean CDA amplitudes (standard deviation) at Time 2: first EEG session and Time 3: second EEG session

Time 3 by group and condition. Note: FE was calculated for each participant individually then averaged for group analysis to account for individual variation in filtering ability.

<table>
<thead>
<tr>
<th>Group</th>
<th>2 item</th>
<th>4 item</th>
<th>Distractor</th>
<th>2 item</th>
<th>4 item</th>
<th>Distractor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Training</td>
<td>-.69 (.80)</td>
<td>-1.10 (.78)</td>
<td>-.93 (.71)</td>
<td>-.77 (.55)</td>
<td>-1.41 (.70)</td>
<td>-1.03 (.61)</td>
</tr>
<tr>
<td>Control</td>
<td>-.54 (.33)</td>
<td>-1.10 (.28)</td>
<td>-.84 (.25)</td>
<td>-.40 (.33)</td>
<td>-.77 (.41)</td>
<td>-.58 (.35)</td>
</tr>
<tr>
<td>Average</td>
<td>-.62 (.52)</td>
<td>-1.10 (.57)</td>
<td>-.89 (.55)</td>
<td>-.58 (.48)</td>
<td>-1.09 (.65)</td>
<td>-.80 (.53)</td>
</tr>
</tbody>
</table>
Figure captions

Figure 1. **Example of a distractor condition in a change trial.** Participants were instructed to remember the orientations of the red rectangles (light grey), ignore the blue rectangles (grey), and respond during the test array with one of two buttons to indicate whether a change was present or not.

Figure 2. **Example of the first three trials in a 1-back block.** Audio and visual stimuli were presented simultaneously. For the 1-back level participants were instructed to remember if the letter spoken or the position square matched that of one trial back. For this example the position of the square in Trial 2 and Trial 3 match. So participants have to press the “A” button for a position match.

Figure 3. **Mean dual n-back level across training day.** Lines indicate standard deviations.

Figure 4. **Grand averaged CDA waveforms for training and control groups at Time 2, pre-test (A) and Time 3, post-test (B).** Each graph shows CDA waveforms (contralateral – ipsilateral activity) by trial condition; 2 item (CDA_2 item), distractor (CDA_Distractor) and 4 item (CDA_4 item). Highlighted region shows analysis window (300ms-900ms).

Figure 5. **Relationship between working memory capacity and filtering efficiency at Time 2, pre-test (A) and Time 3, post-test (B).** Figures show the correlation between working memory capacity and filtering efficiency at Time 2 and Time 3 for training and control groups.
Figure 6. Mean performance gains (post-test minus pre-test) by group for Working Memory Capacity (A) and Filtering Efficiency (B). Figures show mean performance gain (bars) and individual scores in each groups (markers).
Figure 1
Figure 2

Trial 1

Trial 2

Trial 3

Letter Spoken = “C”

Letter Spoken = “K”

Letter Spoken = “R”
Figure 3

Mean dual n-back level across training
Figure 4a

Training Group, Time 2 (pre-test)

Training Group, Time 3 (post-test)
Figure 4b

Control group, Time 2 (pre-test)

Control group, Time 3 (post-test)
Figure 5a

Working Memory Capacity and Filtering Efficiency by Group,
Time 2 (pre-test)

Figure 5b

Working Memory Capacity and Filtering Efficiency by Group,
Time 3 (post-test)